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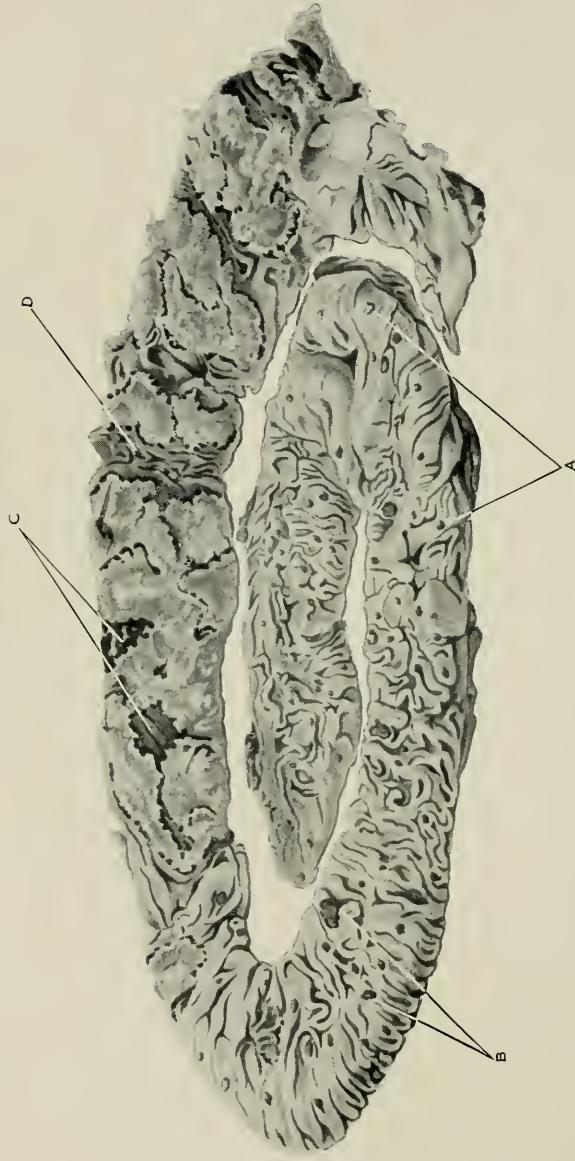
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### LESIONS OF AMEBIC DYSENTERY IN THE GREAT INTESTINE.

- (a) Early stages in cæcum and ascending colon. Buds of proliferating tissue pushing up from the submucosa: suppuration in the central areas of those which are most advanced.
- (b) Ulceration—first stages in the transverse colon.
- (c) Large undermined ulcers with overhanging margins.
- (d) Denuded areas left by sloughing of the mucosa.

*After L. Rogers.*

# AMŒBIC OR TROPICAL DYSENTERY

ITS COMPLICATIONS AND TREATMENT

BY

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## PREFACE.

SINCE Baly chose dysentery as the subject for the Goulstonian Lectures, sixty years ago, there have been many revolutionary changes in our conceptions of disease. At that time dysentery was still prevalent in Great Britain, smouldering for the most part in the slums and hovels of the poorer classes, but occasionally blazing out into virulent epidemics which attacked all sections and grades of society. Thanks to hygienic reform and progress, domestic interest in the condition has considerably narrowed ; for, although infection still lurks in the western districts of Scotland and Ireland, and lingers with a strange persistence in many of our most efficient lunatic asylums, dysentery has been practically banished from the general life of England.

From an Imperial and Colonial point of view, however, the study of this disease still remains a subject of pre-eminent importance. The recent development of industrial and agricultural activities in our tropical possessions and the increased facilities for communication have resulted in an enormous demand for the services of Europeans, and within the last thirty years the white population has multiplied five-fold. Of the protean climatic diseases which they have still to face, dysentery is second in prevalence only to malaria, and from all classes and races it annually claims an appalling number of victims.

The discovery that dysentery itself is not a single disease may be regarded as one of the most remarkable advances in modern medical science ; for, although in medicine it is impossible to claim that any theory of disease has been immutably settled, or that the

final word has been spoken, our conception of amœbic dysentery as a distinct and specific affection is definite and assured, and the pathology of the disorder is now a *chose jugée*. The literature of the subject, already very extensive, is rapidly increasing, and almost every month important additions are being made to our knowledge. The very scope and volume of these contributions is indeed so great that it tends to diminish their practical value ; for, published as they are in all languages and in all parts of the world, and scattered through an enormous number of scientific journals, most of them are accessible only to those who make a special study of the subject. It is believed, therefore, that a general survey of the information which has recently been acquired with regard to amœbic dysentery and other protozoan infections of the human intestine may not be devoid of interest and utility.

For an accurate appreciation of the pathology of amœbic dysentery, a knowledge of the cardinal facts in the life-history of the specific organisms and of their relations to other intestinal protozoa is essential ; and it is endeavoured in these pages to set forth as clearly as possible the outstanding features in the natural history of the entamœbæ. But no attempt has been made to give a complete account of this important group, or to trespass on the domain of pure zoology, and only those events in the development and reproduction of the parasites which have a direct bearing on amœbic dysentery have been fully considered. It is not pretended that the biological section is more than a narrative of the prominent phenomena for which a special relation to a distinct morbid process is claimed ; and, as far as possible, the intricacies of detailed zoological description, which occasionally tend to obscure medical issues, have been avoided.

The book is, indeed, chiefly intended for the practising physician, and its principal aim is to emphasize the necessity of early diagnosis

and to lay down precise and comprehensible directions for the treatment of the various clinical types of amœbic dysentery. An attempt has been made to take into account the varying conditions under which the disease may have to be treated, and special regard is paid to the remedial measures which are best suited to the requirements of warm climates. The object of the work will be more than achieved if the instructions for the general management of cases and for the selection and use of suitable remedies prove of practical value and assistance.

I am indebted to Mr. A. Engel Terzi for the care and artistic skill which he has devoted to the illustrations, and to Miss May Sinclair for many valuable suggestions and much helpful criticism during the revision of the proofs.

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PART I.—GENERAL.



# AMŒBIC DYSENTERY.

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## CHAPTER I.

### INTRODUCTORY.

FOR many centuries, several different infections, similar in their clinical manifestations, but distinct in specific character, have been described by the single term DYSENTERY. The symptoms common to these disorders are definite and characteristic, and clearly separate the condition from other morbid processes of the alimentary tract ; but, within the last few years, the suspicion—originally raised by marked variations in clinical type—that dysentery might itself be more than a single pathological unit, has been fully confirmed.

The number of individual diseases which may rightly be comprised in the group is still uncertain, but at least two have now been definitely differentiated, and the pathogenic nature of the micro-organisms in which they originate has been completely established. Of these infections, one is protozoan, and the other bacterial ; the varieties of dysentery, of which they are respectively the causes, being known as amoebic and bacillary.

Strong claims have been advanced for the further subdivision of these types, and especially for the recognition of additional forms of protozoan dysentery ; but although the evidence which has been adduced is highly significant, it is at present insufficient to warrant

a new classification, or to incriminate other microbial organisms as pathogenic. There is, however, abundant proof of the etiological relation of the rhizopod—*Amœba dysenteriae* (COUNCILMAN and LAFLEUR), *Entamœba coli* (CASAGRANDE), *E. histolytica* (SCHAUDINN)—to amœbic dysentery; and of the connection between one or more species of bacteria—of which the variety known as Shiga-Kruse is the most familiar—and the bacillary variety of the disease.

It is with the first of these infections—Amœbic Dysentery—that this work is principally concerned; and an endeavour will be made to describe the biological relations of the organism, the history of its discovery, the epidemiology and distribution of the disease, the pathological results of amœbic infection, and the most effective methods of prevention and treatment.

**DESCRIPTIVE DEFINITION.**—AMŒBIC DYSENTERY is a disease which originates in penetration and subsequent destruction of the intestinal walls by a specific protozoan micro-organism—*Entamœba histolytica*; the lower segment of the alimentary tract, viz.:—the colon, sigmoid flexure and rectum being the favourite sites of invasion. The signs of acute infection are fever, sickness, pain, and tenesmus, with frequent calls to stool. The dejecta are scanty, and consist principally of mucus and blood.

The commencement of amœbic dysentery is, however, generally very insidious, and active dysenteric symptoms seldom develop for some time after infection. The course of the disease is protracted, and it has a marked tendency to recurrence and chronicity. The later stages are often characterized by toxæmia; and, not infrequently, they are complicated by hepatic suppuration.

**NOMENCLATURE.**—ALTERNATIVE TERMS: TROPICAL DYSENTERY—AMŒBIASIS—AMŒBIC ENTERITIS—AMŒBIC COLITIS—AMÖBENRUHR—DYSENTERIE AMIBIENNE—DYSENTERIE À AMIBES.

As infection by a specific micro-organism of the *Amœba* family is not only the cause of a definite train of symptoms but also serves to distinguish the type of disease, the term *Amœbic Dysentery* is, perhaps, more applicable than any other title. It is eminently desirable that a disorder of widespread prevalence should be known by a distinctive and practical name, and one which is readily comprehensible by laymen as well as by physicians. *Amœbic Dysentery* fulfils these indications satisfactorily; and it has, besides, the conspicuous advantage that it has already secured general adoption.

Considerable confusion has, however, arisen in the nomenclature of the disease by a difference of opinion as to the use of the term "*Tropical*" dysentery. By many writers that name is applied, irrespectively of the nature of the infection, to any variety of dysentery which has originated in the tropics; while by others its application is strictly confined to the *amœbic* type of the disease. *Amœbic dysentery* is, indeed, regularly described by many authorities as "*Tropical*" dysentery, although the reference is to an infection contracted in a cold climate, and although the patient may not have been in the tropics.

This indiscriminate application of the term "*Tropical*" is somewhat unfortunate. Bacterial dysentery is common in the tropics; indeed, although it has become endemic in many temperate regions, it is, essentially, a tropical disease; and many, if not most, of the European invalids who return from warm climates suffering from a chronic flux of mucus and blood exhibit no trace of *amœbic* infection. *Amœbic dysentery*, on the other hand, is by no means a distinctively tropical affection; it is prevalent in most sub-tropical countries, and it is of common occurrence in many districts of the temperate zone.

Strictly speaking, therefore, "*Tropical dysentery*" is an inappro-

pritate title ; but greater confusion undoubtedly results from its employment in a geographical sense than by its retention as a synonymous term for amœbic dysentery. In the latter relation, the name "tropical" has, to a certain extent, been sanctioned by custom ; and, provided that it is applied only to cases of amœbic dysentery, there can be no serious objection to its use.

AMŒBIASIS—a word recently introduced to denote amœbic disease generally—has been adopted by several authors as an alternative title for amœbic dysentery. In this sense, however, it is vague and unsatisfactory ; it does not express the dysenteric state, and it should be confined to cases in which symptoms other than those of dysentery have been produced by amœbic infection. Further confusion is caused by the fact that "amœbiasis" is often applied to the condition in which non-pathogenic amœbæ are harboured in the intestine without hurt to their host ; but its use in this sense is unjustifiable and misleading.

On the other hand, "amœbiasis" accurately and conveniently expresses a morbid state in which amœbic infection is followed by symptoms of which dysentery is not a predominant feature. Such an event is unusual ; but hepatic and cerebral amœbic abscesses, and other consequences of infection, without precedent dysentery, are by no means unknown.

The term AMŒBIC COLITIS is sometimes employed by physicians who find a distinction between colitis and dysentery. In rare instances the development of pathogenic amœbæ may be arrested before the ulcerative stage of inflammation is reached, and "amœbic colitis" would then be descriptive of the pathological condition. But amœbic colitis is, after all, only a stage of dysentery, and a multiplication of names for a single disease is undesirable.



## CHAPTER II.

### HISTORY AND LITERATURE OF AMŒBIC DYSENTERY.

ALTHOUGH various protozoan organisms had previously been described as occasional habitants of the human alimentary tract, the history of amœbic dysentery definitely begins with the discovery by LAMBL of a rhizopod in intestinal mucus, taken from a Jewish child, who died of infantile diarrhœa at the Kinder Spitale in Prague, in 1859. This organism he regarded as a monad—the term then generally used for unicellular protozoa—and his description states that it measured  $\cdot 009$  mm. by  $\cdot 016$  mm. At rest, it was roughly spherical in shape, but when in motion the body became elongated, and the animal progressed by throwing out club-shaped pseudopodia, which were homogeneous with the body substance. LAMBL further noted the characteristic molecular vibration of granules in the protoplasm, which, he stated, was most active near the roots of the pseudopodia. Vacuoles were also seen in the body substance, and, in some specimens, delicate nuclear vesicles were visible. The movements, both protoplasmic and granular, were active at first, but within a few hours after the collection of the intestinal mucus they gradually ceased. These organisms were subsequently demonstrated by the same observer in many other cases of dysenteric diarrhœa.

LAMBL does not appear to have received the credit which he deserved for these important observations. It is generally stated that he attached no pathological significance to the presence of

amœbæ, but that is incorrect. If his original paper is consulted, the following words will be found: "It is an established fact that minute organisms, which appear to be closely related to the rhizopoda, are present in the human intestinal canal, and their importance in regard to the concomitant pathological processes in children should certainly not be under-rated."<sup>1</sup> Not only, therefore, did LAMBL first describe the morphology of an intestinal amœba, but he demonstrated the organism in association with a definite form of disease, and although he naturally hesitated to express the view that pathogenicity had been proved, he clearly realized that it was probable.

LAMBL'S researches were published in a somewhat inaccessible series of reports, and, although noted<sup>2</sup> by LEUCKART (who also found parasitic amœbæ in the human intestine), his paper failed to reach other investigators. In India, LEWIS, while examining cholera dejecta in 1870, observed living amœbæ, but attached no importance to their presence, and although his description of the organisms is full and distinctive, it is not clear that he even recognized them as protozoa. He seems rather to have regarded them as some variety of normal cell, the morphology and development of which resembled that of an ordinary leucocyte. There can be little doubt, however, that if LEWIS had been aware of LAMBL'S paper, he would have taken a different view, and would have made further inquiry into the subject of amœbic infection.

Five years later, intestinal amœbæ were again demonstrated and described by Dr. F. LÖSCH, clinical assistant to Professor Eichwald, of St. Petersburg. The patient was a young peasant

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<sup>1</sup> Lambl, "Beobachtungen und Studien aus dem Gebiete der pathologischen Anatomie und Histologie." Prague: 1860, Friedrich Tempski.

<sup>2</sup> F. Leuckart, "Die menschlichen Parasiten." 1863.

of Archangel, who was suffering from dysentery which, after persisting intermittently for two years, ultimately proved fatal. During his illness, amœbæ were repeatedly found in the mucus passed with the dejecta; but just before death, which was actually the result of a terminal pleuro-pneumonia, the organisms entirely disappeared. At the *post-mortem* examination, however, they were shown to be present in enormous numbers in the intestinal contents, and in numerous ulcers on the mucous membrane of the colon and sigmoid flexure.

LÖSCH, who had seen LAMBL'S paper and was much impressed by his researches, fully appreciated the pathological importance of the discovery. But, clear as was the evidence, it was supplied by a single instance of the disease, and was still insufficient to establish a claim for pathogenicity. He accordingly limited himself to the conclusion that a superimposed infection of amœbæ had possibly only aggravated an ordinary case of ulcerative colitis. His own belief is, however, clearly indicated by the fact that he undertook experiments to test the biological relations of the organisms. Some mucus containing amœbæ was injected into the rectal cavities of four dogs, and in one case this attempt to reproduce the disease was successful, for dysentery supervened, and amœbæ were recovered from the dejecta. The infected dog, when killed, was found to be suffering from extensive, although superficial, ulceration of the lower part of the colon.

There can be no doubt that LÖSCH'S case was a typical instance of amœbic infection, and his careful study of the condition,<sup>3</sup> illustrated as it is by a large number of excellent plates, which show the development of the amœba and its power of ingesting red

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<sup>3</sup> F. Lösch, "Massenhafte Entwicklung von Amöben im Dickdarm," *Virchow's Archives*, lxx., 156.

blood corpuscles, remains one of the best, as it is the first important contribution to the literature of amœbic dysentery.

Closer attention was naturally directed to the subject of intestinal amœbæ by the publication of LÖSCH's report, and during the next few years numerous papers on the development and life-history of parasitic protozoa appeared in medical and scientific journals. Among the more important were those of GRASSI,<sup>4</sup> who, so early as 1879, showed that intestinal amœbæ passed through a cystic stage, and that, when the conditions of life were unfavourable, cysts were formed in greater numbers. He found intestinal amœbæ in healthy persons as well as in those affected by dysentery, and he accordingly opposed the theory advanced by LÖSCH that they might be the cause of the disease.

About the same time, amœbæ were reported by LEUCKART<sup>5</sup> as having been found in healthy human dejecta, by PERRONCITO<sup>6</sup> as occurring in the contents of an otherwise normal colon, and by SONSINO<sup>7</sup> (who, however, did not regard them as causative) in the intestinal mucus of a child who died of dysentery at Cairo.

From that city also came the next important addition to the knowledge of the subject. While examining sections made from the intestinal walls of victims of the cholera epidemic of 1893, Professor KOCH observed a species of amœba embedded in the tissues. This he regarded as possibly pathogenic, but, being fully occupied with bacteriological work, he was unable at the time

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<sup>4</sup> Grassi, "Die protozoi parassiti e specialmente di quelle che sono nell'uomo," *Gazeta Med. Italiana*, 1879, p. 445; and other papers in the Proceedings of the *Società Italiana di scienza naturale*, Milan, 1882; and in the *Atti de R. Accademia di Lincei*, 1888.

<sup>5</sup> Leuckart, "Die Parasiten des Menschen." Leipzig, 1879.

<sup>6</sup> Perroncito, "I Parassiti." Milano, 1881.

<sup>7</sup> P. Sorsino, "Davidson's Hygiene and Diseases of Warm Climates." 1893.

to investigate the question, and he asked Dr. S. KARTULIS to determine, if possible, whether the organism had any definite relation to a morbid process.

During the next two years, KARTULIS examined, *post mortem*, a large number of fatal cases of intestinal disease, and, as a result of his observations, published <sup>8</sup> several papers in which he stated that amœbæ were invariably found in Egyptian dysentery; and he further recorded his belief that they were undoubtedly the pathogenic agency in that disease.

In a consecutive series of 150 autopsies, which he made at the Greek and Arab hospitals in Cairo, KARTULIS found amœbæ in every instance in which there had been marked dysenteric symptoms, whilst in patients who had died from other causes they were never once discovered. He thought that in severe dysentery the amœbic infection was excessive, and that in mild cases it was slight, and he claimed that a direct relationship between the number of organisms and the intensity of the symptoms could always be demonstrated.

Of twelve fatal cases of dysentery in which sections of the colon were made, amœbæ were found in every one; while similar specimens prepared from the intestines of thirty persons who had died of typhus, tuberculosis, enteric fever, and Bilharzia disease, contained not a single amœba. KARTULIS was unable at the time to cultivate the amœba, or to reproduce the disorder in guinea-pigs and rabbits; but his experiments in this direction were on a scale insufficient to give reliable results.

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<sup>8</sup> Kartulis, "Ueber Riesen-Amöben bei chronischer Darmentzündung der Aegypter," *Virchow's Archives*, 1885, xcix., 145.

*Idem*, "Zur Aetiologie der Dysenterie in Aegypten," *Virchow's Archives*, 1886, cv., 521.

*Idem*, "Einiges über die Pathogenese der Dysenterie," *Centralbl. für Bakt.*, 1891, ix., 365.



There can be no question of the importance of those observations, and of the influence which they exercised on the views then current as to the nature of the disease. Since the days of Hippocrates, dysentery had been regarded as a "phlegmonous" or "sthenic" inflammation; and the proper method of dealing with it was believed to be depletion and the continued action of depressant drugs. The introduction of ipecacuanha had lessened, to some extent, the appalling mortality which had long been considered inevitable, but which, it was now realized, was a direct consequence of treatment. Still, although blood-letting to faintness and huge doses of calomel had given place to more rational remedies, the conception that dysenteric symptoms might originate in various causes, and that at least one variety of dysentery was parasitic, came as a revelation. The ultimate establishment of amœbic dysentery as a distinctive disease is largely due to KARTULIS's pioneer work in Egypt; and he may justly claim the greatest share of the credit for this notable advance in medical science.

KARTULIS has elaborated and confirmed these researches by many further observations. In 1887 he pointed out the definite association of *Amœba coli* with hepatic suppuration; and he has since published<sup>9</sup> numerous important papers on amœbic dysentery and its sequelæ. The recent article, "Die Amöben Dysenterie," in KOLLE and WASSERMANN'S "Handbuch"—an excellent and comprehensive review of the subject—is from his pen.

KARTULIS'S observations were promptly confirmed by HLAVA<sup>10</sup>

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<sup>9</sup> See among others: (1) "Ueber weitere Gebreitungsgebiete der Dysenterie-Amöben," *Centralbl. f. Bakt. und Parasitenkunde*, 1891, ix.; (2) "Ueber pathogene Protozoen bei dem Menschen," *Zeitsch. f. Hygiene*, Bd. xiii., F. 2; (3) "Gehirn Abszesse nach Dysenterie Leber Abszesse," *Centralbl. f. Bakt.*, 1904, xxxvii., 527; (4) Kolle and Wassermann: G. Fischer, Jena, 1907.

<sup>10</sup> Hlava, *Centralbl. f. Bakt.*, 1887, i., 527, Ungarn.

at Prague; but in Europe and the tropics they attracted little attention. In America, however, the articles in *Virchow's Archives* had been noted by Osler, who thereupon instituted a search for amœbæ in the cases of dysentery which happened at the time to be under his care. One patient who had returned from Panama, and who was being treated for chronic dysentery in hospital at Baltimore, was found to be passing large numbers of amœbæ; and several other instances of amœbic infection were subsequently reported from different parts of the United States.

Further cases in Professor OSLER'S wards at Baltimore furnished material for a very complete study of amœbic dysentery by Drs. COUNCILMAN and LAFLEUR.<sup>11</sup> Their account of the disorder, published in 1891, combines an excellent description of the symptoms and pathology of amœbic infection with a comprehensive and critical review of the literature of dysentery—the *post-mortem* records left by Indian and other tropical pathologists being specially subjected to examination with reference to the indications they afford as to the possible duality of the disease.

There is much evidence to that effect scattered through the writings of the older medical authorities. So long ago as 1828, ANNESLEY,<sup>12</sup> of Madras, divided dysentery into several different classes; and, noting the frequent association of thickening and ulceration of the great intestine with inflammation of the liver, he named one of the most familiar types "Hepatic dysentery." He, however, misinterpreted the pathological connection, and regarded the dysenteric condition as a consequence of disordered secretion of bile. DUTROLAU,<sup>13</sup> also, had insisted that tropical dysentery

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<sup>11</sup> Councilman and Lafleur, *Johns Hopkins Hospital Reports*, 1891, ii.

<sup>12</sup> Annesley, "Researches into the Diseases of India." London, 1841.

<sup>13</sup> Dutrolau, "Maladies des Européens en Pays chauds." Paris, 1868.

differed widely, both in symptoms and pathology, from the hæmorrhagic flux of temperate climates. In this view he was supported by most of his contemporaries; and there are numerous other indications that, in certain parts of the world, amœbic dysentery has, from the earliest times, been a prevalent, although unsuspected disease.

Not the least important of COUNCILMAN and LAFLEUR'S results was an observation which indicated the existence of two varieties of amœbæ, differing in appearance and in pathogenic virulence. These they named *A. dysentericæ* and *A. coli*. Their closely reasoned argument that amœbic dysentery deserved recognition as a separate disease was widely read and discussed, with the result that the whole subject was carefully re-investigated; and numerous important articles by zoologists and physicians were published during the next two or three years. Some of these writers<sup>14</sup> confirmed and extended the views of COUNCILMAN and LAFLEUR; but others<sup>15</sup>—and, indeed, the greater number—refused to accept their work, and vehemently opposed the theory of pathogenicity in any variety of amœba.

In this controversy, which was carried on with much vigour both in America and on the Continent, English physicians, who formed the great majority of tropical workers, took no definite side; but it is a curious fact that, while foreign pathologists, as a rule, favoured the doctrine of specific pathogenicity, biologists (with the notable exception of SCHAUDINN), almost to a man, denied that the parasitic amœbæ exercised any pathological influence on their hosts.

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<sup>14</sup> See, among others: A. Kovacs, "Beobachtung und Versuche ueber Amöben Dysenterie," *Zeitsch. f. Heilk.*, 1892, xiii., p. 509.

<sup>15</sup> See, among others: A. Schuberg, "Die parasitischen Amöben des menschlichen Darms," *Centralb. f. Bakt.*, 1893, xiii., pp. 18, 22.



Much of the adverse criticism was naturally based on the facts—already noted by CUNNINGHAM, PERRONCITO, GRASSI, MASSIUTIN, and others, that amœbæ were frequently present in the contents of the normal intestine; and that experiments, such as those of CALANDRUCÉIO,<sup>16</sup> showed that encysted amœbæ might be swallowed without ill-effect, although an abundant development of living amœbæ took place immediately after they were ingested.

In 1893, MAGGIORA,<sup>17</sup> after a careful review of all the evidence then available, concluded that no cause had been shown for the incrimination of *Amœba coli* as the pathogenic agent in any variety of dysentery; and GASSER,<sup>18</sup> by the injection of garden mould, not only induced active colitis in cats, but recovered amœbæ, apparently identical with those of LÖSCH and KARTULIS, from their excreta; while SORGA further showed that the introduction of dysenteric matter, which had been proved to be free from amœbæ, could induce dysentery both in man and animals, and that amœbic organisms might sometimes be found in the resultant dejecta.

Further light was thrown on the question of pathogenicity by H. QUINCKE and E. ROOS,<sup>19</sup> whose work, at Kiel, to some extent anticipates the later discoveries of SCHAUDINN. In two cases of chronic dysentery, one of which had been contracted at Palermo, or, possibly, in Egypt, and the other certainly in Schleswig-Holstein, they found amœbæ, which varied in appearance, both in their active and encysted state, and which differed also in their method of reproduction. The organisms harboured by the first patient

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<sup>16</sup> Calandruccio, *Atti. Accad. Giorn.*, 1890, ii., p. 95.

<sup>17</sup> A. Maggiora, *Centralbl. f. Bakt. und Parasitenkunde*, Jena, 1892, 173.

<sup>18</sup> J. Gasser, "Note sur les causes de la dysenterie," *Archives de Médecine exp. et d'Anat. path.*, 1895, ii., 198.

<sup>19</sup> Quincke and Roos, "Ueber Amœben Enteritis," *Berlin. klin. Wochenschr.* 1893, 1089.

were apparently identical with those described by COUNCILMAN and LAFLEUR, and the dysenteric symptoms were severe ; in the second instance the amœbæ were larger, the nucleus being less clearly defined, and they were associated with flagellated protozoa. In this case the disorder was comparatively trivial.

As a result of these observations, QUINCKE and ROOS concluded that there were at least two varieties of pathogenic amœbæ, one of which—the tropical or Egyptian—was more virulent than the other. The latter organism they believed to be a species peculiar to cold countries, and productive of a milder type of dysentery.

They further claimed that still another variety of amœba could be differentiated, and that it was composed solely of parasitic, but non-pathogenic organisms. Amœbæ recovered from the dejecta of nine out of twenty-four healthy persons to whom a purgative had been previously administered, were found to be different from either of the species noted in dysentery ; and QUINCKE and ROOS supported this observation by experiments which showed that, when injected into the rectum, their first organism was highly pathogenic to cats, but that the second and third varieties failed to cause dysentery.

Soon afterwards, Dr. W. KRUSE, of the Hygienic Institute in Berlin, and Staff-Surgeon ALESSANDRO PASQUALE, of the Royal Italian Navy, undertook a journey to Egypt in order to test the theory of pathogenicity by further investigation and experiment. Working principally at the Greek Hospital in Alexandria, Drs. KRUSE and PASQUALE were able<sup>20</sup> to corroborate almost the whole of COUNCILMAN and LAFLEUR's observations. They specially verified the statements of these authors as to the existence of both

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<sup>20</sup> W. Kruse and A. Pasquale, "Eine Expedition nach Egypten zum Studium der Dysenterie und Leberabzess," *Deutsch. med. Wochenschr.*, 1893, 354.

a pathogenic and a harmless species of intestinal amœba; and it is interesting to note that their description of the former closely agrees with that of *Entamœba histolytica* afterwards given by SCHAUDINN.

In the hands of KRUSE and PASQUALE, reproduction experiments, which had previously given somewhat ambiguous results, were highly successful; and they were the first to prove that amœba-containing pus from a hepatic abscess (although otherwise sterile), if injected into the lower intestines of cats, may induce true amœbic dysentery. The result of their detailed investigation of fifty cases of the disease was to give an unqualified confirmation to the clinical and pathological work of LÖSCH, KARTULIS, COUNCILMAN and LAFLEUR.

Further experiments, however, were less conclusive. A contemporary observer, ZANCAROL of Alexandria, showed<sup>21</sup> that not only could amœbic dysentery and liver abscess be successfully transferred to the domestic animals, but that hepatic pus which had been ascertained to contain no amœbæ, if injected into the rectum of a cat, might set up acute dysentery. He argued from these results that the origin of the disease was streptococcal, and not protozoan.

Soon afterwards Professor CELLI,<sup>22</sup> working in collaboration with R. FIOCCA, published several important memoirs on intestinal protozoa. The amœbæ parasitic in man were divided by these authors into no fewer than six species, none of which were considered to be actually pathogenic. In their review of the work which had been carried out in Egypt and in Italy, CELLI and

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<sup>21</sup> Zancarol, "Pathogénie des Abscès du Foie," *Revue de Chirurgie*, 1893, 677.

<sup>22</sup> A. Celli, *Centralbl. f. Bakt.*, xv. Cf. *ibid.*, 1902, I. Abt.

FIOCCA<sup>23</sup> maintained that all dysentery was really bacterial in origin; and as *Bacillus coli* and *Amœba coli* were so frequently found in symbiosis, they suggested that these organisms exercised a definite influence on each other, and that the development of amœbæ possibly effected a metamorphosis of *B. coli* into *B. dysenteriae*.<sup>24</sup>

Moreover, although generally favouring the claim for pathogenicity, physicians and pathologists were by no means unanimous. In a report,<sup>25</sup> communicated to the Verein für innere Medicin, of Berlin, in January, 1896, Dr. I. BOAS stated that, as the result of a large number of experiments by himself and others, he had come to the conclusion that pathogenicity had not been established. He considered that both the experimental animals and the material used by previous observers were unsatisfactory, and that the results, in consequence, were unreliable.

Soon afterwards—in 1897—Dr. W. JANOWSKI, of Warsaw, contributed a series of papers<sup>26</sup> to the *Centralblatt für Bakteriologie*, which contains an excellent *catalogue raisonné* of previous researches on the etiology of amœbic dysentery. His own observations and experiments to determine the actual pathogenicity of the amœba were somewhat inconclusive, but JANOWSKI considered that the distinction between bacterial and amœbic dysentery had been clearly proved, and that the weight of evidence favoured the view that the latter disease was caused by the combination of a definite species of amœba with bacterial organisms.

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<sup>23</sup> Celli and Fiocca, *Annali d'igiene speriment.*, 1896, vi., 204; "Ueber die Aetiologie der Dysenterie," and other papers in the *Centralbl. f. Bakt.*, xv., xvi., xvii.; "Intorno alla Biologia delle Amœbe," *Bull. R. Accad. Med.*, Rome, 1894-5, and other journals.

<sup>24</sup> Cf., "La Métamorphose dans les Microbes," A. Rodet. Paris: Baillière.

<sup>25</sup> I. Boas, "Amœben Enteritis," *Deutsch. med. Wochenschr.*, 1896, 214.

<sup>26</sup> Janowski, *Centralbl. f. Bakt.*, 1897, xxii., 88, 151, 194, 324.

About the same time (1897) Drs. O. CASAGRANDE and P. BARBAGALLO, of the Zoological Department of the University of Catania, who had already published<sup>27</sup> several articles on the same subject, issued<sup>28</sup> a full account of their researches into the life-history and relations of the intestinal amœbæ. This important study attracted general attention; and, among others, it was noticed by SCHAUDINN, who, although he differed from the main conclusion of the authors that no species of amœba was pathogenic, declared it to be an exact statement of biological fact.

In a further article,<sup>29</sup> Drs. CASAGRANDE and BARBAGALLO dealt with the artificial reproduction of the organisms, and stated their belief that no parasitic amœba had yet been successfully cultivated. The amœbæ which other observers claimed to have grown were, they thought, the result of accidental contamination of cultures by cysts or spores of free-living species.

In the following year (1898) TSUJITANI<sup>30</sup> claimed that although he had been unable to obtain a pure culture, he had successfully grown intestinal amœbæ in symbiosis with the spirillum of cholera; and, as the result of an experiment by which he showed that cysts, sown on a medium on which pathogenic bacteria, while growing, had been previously killed by drying over sulphuric acid, would develop in three to five days, he suggested an interdependent relationship between specific protozoa and virulent bacteria.

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<sup>27</sup> Casagrandi and Barbagallo; see "Ricerche sull' Amœba Coli (Lösch)," *Atti Acad. Med. di Catania*, 1895, and other papers.

<sup>28</sup> *Idem*, "Entamœba Hominis (Amœba Coli), Lösch, Studio biologico e clinico," *Annali igien. sperimentali*, 1897 and 1899. See also *idem*, "Sulla sterilità del pus degli ascessi epatici dei climi caldi," *Gaz. Ospedale Milano*, 1896.

<sup>29</sup> *Idem*, "Ueber die Cultur von Amöben," *Centralbl. f. Bakt.*, 1897, xxi., 579

<sup>30</sup> Tsujitani, "Ueber die Reincultur der Amöben," *Centralbl. f. Bakt.*, 1898, xxiv., 666.



The next paper of note was a clinical and pathological review of thirty-five cases of amœbic dysentery—all of them originating in the Southern United States—which was published<sup>31</sup> by Professor H. F. HARRIS, of the Jefferson Medical College. HARRIS'S description of the symptoms, morbid anatomy and distinctive characteristics of the disease corresponds closely with the accounts of OSLER, and COUNCILMAN and LAFLEUR; and his opinions as to its specific nature are in accord with those of most other American authorities.

During the next few years a considerable number of clinical and pathological observations, generally corroborative of the theory of pathogenicity, were recorded from various parts of the world; but, with the exception of a detailed description of the disease<sup>32</sup> by JÜRGENS, which appeared in 1902, no important addition was made to the literature of amœbic dysentery until the publication of FRITZ SCHAUDINN'S memoir,<sup>33</sup> "Die parasitären Amöben des menschlichen Darmkanals."

The incidents which surround SCHAUDINN'S work during his short stay on the shores of the Adriatic are full of interest. Pending the completion of the Institute of Protozoology in Berlin, of which he had been appointed first director, he was placed in charge of the zoological station at Rovigno, where he immediately undertook an extended series of researches into the life-history and biological relations of the parasites of malaria and dysentery.

In the neighbouring villages both diseases were endemic, and very prevalent; and with the abundance of clinical material which was thus continuously at his disposal, SCHAUDINN was able to

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<sup>31</sup> Harris, "Amœbic Dysentery," *Amer. Journ. of Med. Science*, 1898, cxv., 384. See also "Experim. bei erzeugte Dysenterie," *Virchow's Archives*, 1901.

<sup>32</sup> Jürgens, "Zur Kenntniss der Darmamöben und der Amöben-Enteritis." *Veröffentlichen aus dem Gebiete des Militär-Sanitätswesens*, H. 20, p. 110. Berlin: Hirschwald, 1902.

<sup>33</sup> F. Schaudinn, *Arbeiten aus dem Kaiserlichen Gesundheitsamte*, 1903.

follow his favourite method of investigation by the simultaneous observation of large numbers of fresh specimens. In this way he ascertained almost at once that the conjectures of former observers were correct, and that at least two species of amœba, which differ widely in their morphological characters, in their life-cycles, and in their modes of reproduction, may be parasitic in the human colon. He also showed that one of these organisms, termed by him *Entamœba coli*, was entirely harmless; and that the other, which he named *Entamœba histolytica*, was the definite cause of amœbic dysentery.

SCHAUDINN's work at Rovigno will be remembered not only for its scientific importance, but also on account of the melancholy interest which attaches to one of his investigations. While engaged in testing and comparing the pathogenicity of the different species of amœba, he did not hesitate to infect himself by swallowing the developmental cysts of the organisms; and he had, in consequence, two serious attacks of dysentery. It is, indeed, only too probable that his untimely death was a direct consequence of this disastrous experiment; for, after his return to Germany, he suffered intermittently from dysenteric seizures, and four years later deep suppuration round the sigmoid flexure was attended by a fatal result.

SCHAUDINN's observations removed the chief obstacle to the recognition of amœbic dysentery as a distinct disease, and proved that the pathology of LÖSCH, COUNCILMAN, and KARTULIS was established on an accurate and scientific basis of fact. His discovery explained why a parasite, for which pathogenicity was claimed, had apparently been shown, in many instances, to be merely an innocuous commensal, and to be of frequent occurrence in perfectly healthy individuals; and it satisfactorily answered every argument which had been adduced to prove that intestinal amœbæ played no part in the production of specific disease. The scientific

differentiation of the organisms into two zoological species entirely transformed the significance of all previous observations and experiments, and finally determined the rôle of amœbæ in the causation of dysentery.

Subsequent research has confirmed the accuracy of SCHAUDINN'S work in every important particular. After a careful re-investigation of the whole subject, C. F. CRAIG who with most other American observers, had at first believed<sup>34</sup> that there were insufficient grounds for the specific distinction of entamœbæ, expressed<sup>35</sup> his full concurrence in a biological and clinical differentiation. CRAIG'S later researches, indeed, corroborate and extend SCHAUDINN'S conclusions in a very remarkable manner; and his report constitutes an excellent introduction to a study of our present knowledge of the life-history of the intestinal amœbæ.

In the tropical foyers of the disease, SCHAUDINN'S discoveries, although at first regarded with incredulity, are now accepted by the great majority of scientific observers. Much of the previous work in Manila had, indeed, to some extent at least foreshadowed his results. MUSGRAVE and STRONG<sup>36</sup> had differentiated the pathogenic from the innocuous amœbæ of the intestine by reproduction experiments in cats, and had shown that free-living amœbæ grown in straw infusion were incompetent to produce specific infection. They had also noted morphological differences, and SHIGA<sup>37</sup> had claimed that *Amœba dysenteriae* was distinguished from other varieties by its larger size.

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<sup>34</sup> C. F. Craig, "The Life-cycle of *Amœba coli*," *American Medicine*, February 20, 1904.

<sup>35</sup> *Ibid.*, *American Medicine*, May 27, June 3 and 10, 1905.

<sup>36</sup> R. Strong, article, "Amœbic Dysentery," "System of Medicine," Osler and McCrae, vol. i.

Musgrave and Clegg, "Amebas: their Cultivation and Ætiological Significance," No. 18, Bureau of Government Laboratories, Manila.

<sup>37</sup> K. Shiga, *Centralbl. f. Bakt.*, xxxii., 352.



MUSGRAVE, however, still finds himself unable to accept in their entirety SCHAUDINN'S views as to the specific distinction of *Entamœba histolytica*, and, whilst admitting the general accuracy of his statements, he and CLEGG<sup>38</sup> hold staunchly to their original opinion that all species of intestinal amœbæ are potentially pathogenic; that every individual who harbours amœbæ of any variety may be regarded as suffering from amœbiasis; and that all or any of these organisms, irrespective of their morphological characteristics, are possible causes of amœbic dysentery.

No material addition to our knowledge of the disease has been made since the publication of SCHAUDINN'S article in the *Arbeiten aus dem Kaiserlichen Gesundheitsamte*, but important papers, most of them confirmatory of his work, have been issued in India by ROGERS,<sup>39</sup> ANDERSON,<sup>40</sup> and others; by CLEGG, WOOLLEY,<sup>41</sup> (both of them in collaboration with MUSGRAVE), and FLEXNER<sup>42</sup> in America; by DOPTER,<sup>43</sup> PRUËS,<sup>44</sup> and other writers in France; by VIERECK,<sup>45</sup> JÜRGENS,<sup>46</sup> and KARTULIS<sup>47</sup> in Germany; and by SAUNDBY,<sup>48</sup> MILLER, and others in England.

<sup>38</sup> Musgrave and Clegg, *Philippine Journal of Science*, ix., 1.

<sup>39</sup> L. Rogers, *Brit. Med. Journ.*, November, 1905, and June, 1906.

<sup>40</sup> A. R. S. Anderson, *Indian Medical Gazette*, April, 1907; *Brit. Med. Journ.* 1908, ii., 1243.

<sup>41</sup> Woolley and Musgrave, *Journ. Amer. Med. Assoc.*, 1905.

<sup>42</sup> S. Flexner, article, "Amœbic Dysentery," Clifford Allbutt's "System of Medicine." 1907.

<sup>43</sup> Ch. Dopter, "Les Dysenteries," Paris, 1908: Octave Doin. Also *Archives de Médecine Expérimentale*, July, 1907.

<sup>44</sup> Henri Pruës, "Dysenterie Amibienne." Toulouse, 1905.

<sup>45</sup> H. Viereck, "Studien über in dem Tropen erworbene Dysenterie," Beihefte. Barth, Leipzig, 1907.

<sup>46</sup> Jürgens, "Die Amöben-Enteritis," *Zeitsch. f. exp. Path.*, December, 1907.

<sup>47</sup> S. Kartulis, "Die Amöben-Dysenterie," Kolle and Wassermann's "Handbuch." Jena: G. Fischer, 1907.

<sup>48</sup> Saundby and Miller, "A Case of Amœbic Dysentery," *Brit. Med. Journ.*, March, 1909.

## CHAPTER III.

### EPIDEMIOLOGY AND GEOGRAPHICAL DISTRIBUTION.

ONLY in very few places has there been any scientific investigation of the epidemiology of amœbic infection, but a good idea of the general distribution and preferential tendencies of the different types of dysentery may be gained by a comparison of the relative frequency of the amœbic and bacillary forms of the disease in Japan and the Philippine Islands. In both of these endemic centres the subject has been carefully studied, and, as a large body of statistical evidence is now available, the results may be regarded as accurate and reliable.

The extreme southern districts of Japan reach to within  $22^{\circ}$  of the Line; but this tropical area is of limited extent, and the continental part of the Japanese archipelago lies almost entirely in the temperate zone. The Philippine Islands, on the other hand, are altogether tropical. Both countries offer unusually favourable conditions for the development and spread of epidemic dysentery; population is everywhere dense, sanitation defective, and pollution of food and water supplies widespread and continuous. In the Philippines, amœbic dysentery is perhaps the commonest of all the serious diseases which affect the inhabitants of the islands. Its frequency relatively to other types of dysentery is probably higher than in any other part of the world, and, although all classes of the community are attacked, Europeans are especially

liable to infection. Dr. COOK, of the Government Civil Hospital in Manila, states that 30 per cent. of the patients treated at that institution suffer from amœbic infection. Fifty out of every thousand native inhabitants annually contract dysentery, and five of that number succumb to the disease.

An estimate of the relative incidence of the different types may be formed from the following statistics: At autopsies made in Manila, during the year 1900, on 147 fatal cases of dysentery, it was proved that 67 per cent. of them were amœbic; whilst, of 1,327 patients examined by STRONG and MUSGRAVE, 561 or 42 per cent. were found to be suffering from the same infection. The incidence, indeed, appears to be increasing, for the average proportion of amœbic cases is, at present, no less than 80 per cent., and in 90 out of every 100 fatal cases of dysentery amœbic lesions may be demonstrated.<sup>1</sup>

Amœbic disorders of the intestines appear to be especially prevalent among the American forces stationed in the Philippines. A series of 300 observations carried out at the Canaço Naval Hospital by E. R. HOYT, in 1907,<sup>2</sup> showed that of all the officers and men admitted for treatment (cases diagnosed as dysentery excluded), 30 per cent. harboured motile entamœbæ, and 15 per cent. intestinal flagellates. In 14 or 70 per cent. of the 20 cases admitted as dysentery, motile entamœbæ were present, and in 20 per cent. of the remainder encysted organisms were found. Prolonged service on the station appeared to increase the liability to infection.

To these figures Japan presents a marked contrast. There, also,

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<sup>1</sup> R. Strong, "Amœbic Dysentery," Osler and McCrae's "System of Medicine," i., 488, and other articles.

<sup>2</sup> E. R. Hoyt, *Philippine Journal of Science*, iii., No. 5 (1908).

dysentery has long been rampant, and the older histories of the Empire contain numerous references to calamitous epidemics of the disease, which visited the country at more or less regular intervals and carried off innumerable victims. These traditions are by no means imaginary, and they have recently been corroborated in a remarkable manner by the accurate statistics which are being collected for the Japanese Government. In a Report on the Epidemiology of Dysentery in Japan, SHIGA<sup>3</sup> has shown that from time to time within the last thirty years the disease, ever present in endemic form, has suddenly and periodically assumed a grave epidemic type. On these occasions extension was always in a definite direction, and almost invariably from south to north. In the earlier periods of the outbreaks, the ratio, both of case incidence and of fatality, was appalling, but after some time the fastigium appeared to be reached, and statistics again assumed a more normal level. The cycle of recurrence is stated by SHIGA to be about ten years.

In Japan, the normal incidence of dysentery is about 50,000 cases annually, with 11,000 or 12,000 deaths; but when the disease becomes epidemic these figures are greatly increased. In 1883, and again in 1893, severe outbreaks occurred in Kiushu, Shikoku, and the central provinces. During the latter year there were, in Kiushu alone, 50,000 deaths; and in Shikoku 135,000 cases. Throughout the whole of Japan, the enormous number of 875,000 cases of dysentery are stated by SHIGA to have been reported during the decade 1890-1900; and of these no less than 231,000 were fatal, a case mortality of over 26 per cent.

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<sup>3</sup> K. Shiga (translated by Thoinot), "Epidémiologie Dysentérique en Japon," *Archives de Médecine Navales*, Octobre, 1906. See also K. Shiga, "Epidemiologische Betrachtungen über die Dysenterie in Japan," *Zeits. f. Hyg. und Infekt. Krankh.*, 1908, 75-92, and *Philippine Journ. of Science*, 1906, 396.

There can be no doubt as to the type of dysentery which is responsible for those epidemics. Japanese observers are unanimous in declaring that it is always bacillary, that amœbic dysentery is never seen in epidemic form, and that, except in<sup>4</sup> Formosa and the extreme southern provinces, the latter disorder is rare in Japan.

In North and Central China, although accurate statistics are unobtainable, it is probable that the epidemiology of the disease is closely similar to that of Japan. Dysentery is always prevalent; periodically it becomes epidemic, and the clinical type is acute and virulent. In these districts, the usual infection is, no doubt, bacillary; but, on the other hand, the endemic dysentery of South China, Hong Kong, and the Treaty ports, in the great majority of instances, is amœbic.<sup>5</sup> The chronic dysentery from which European residents on the China coast so frequently suffer is almost invariably of the latter type.

In Cochin China, in the French dependencies in Further India, and in Siam, dysentery is responsible for more than a third of the total number of deaths. Considerable difference of opinion, however, exists<sup>6</sup> as to the actual nature of the affection. It is certain that many deaths which are reported as being due to dysentery are, in fact, the result of sprue—the endemic diarrhœa of Cochin China—and that many others are caused by bacillary infections; but it is significant that, when amœbic dysentery is looked for, it is generally

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<sup>4</sup> Nakagawa, "Ueber Urheber der in Formosa endemischen Dysenterie," *Mitteil. de medicin. Gesell.* Tokio, 1907. Also Shiga, *Centralbl. f. Bakt.*, various papers, 1898, 1902.

<sup>5</sup> Jürgens, *Veröff. a. d. Gebiet, d. Militär Sanitätswesen*, 1902, H. 20; "Die Amöben-Enteritis und ihre Beziehungen zur Dysenterie," *Zeits. f. exp. Path.*, 1907, 4, 3.

<sup>6</sup> See Pfühl, *Archives de Médecine Navales*, 1906, 401, and many other French writers on the Endemic Diarrhœa of Cochin China. Also, Ruge in Mense's "Tropenkrankheiten."

found, and a careful examination of a recent series of cases of dysentery, which occurred amongst the crews of the French Naval Squadron stationed in these waters during the years 1904-05, resulted in 30 per cent. being classed as amœbic. Of the invalids suffering from dysentery who are sent home to France for treatment, a still greater proportion are affected by the amœbic form of the disorder; and more than half of all the cases which occur in Europeans in civil employment are of amœbic origin.

In Siam, amœbic disease is very prevalent. Of fifty cases of dysentery which were examined in the prison hospital at Bangkok, WOOLLEY found<sup>7</sup> amœbæ in eleven, or 22 per cent.; and he further reports that of a total population of eight Europeans in a small town of 4,000 inhabitants in Lower Siam, four suffered from amœbic dysentery in one season.

The British and Dutch East Indies are noted endemic centres of dysentery; and the amœbic form of the disease is especially prevalent throughout the whole of the tropical districts of Eastern Asia and the Eastern Archipelago. Here, as in South China, the clinical characteristics of the different varieties are exceptionally well marked, the chronic and recurrent types being, almost invariably, amœbic; the acute and malignant cases, bacillary. The amœbic variety, too, is the more fatal; for, although large numbers of deaths occur during acute attacks, a still greater proportion of fatalities must be ascribed to toxæmia and exhaustion, induced by protracted illness and repeated relapses.

In the Malay Peninsula and Sumatra, 50 per cent. of all cases of dysentery are amœbic; whilst in Java, Celebes, and the islands of the East Indian Archipelago the proportion is even higher.

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<sup>7</sup> Paul G. Woolley, *Journ. of the Amer. Med. Assoc.*, October 9, 1906, and private communication.



In India, amœbic dysentery, although less prevalent than in Eastern Asia, is widely but irregularly distributed, some districts being much more severely affected than others. In Madras, Pondicherri, Mysore, Travancore, Haidarabad, and Malabar<sup>8</sup> it is very common; whilst, in Bombay, POWELL states<sup>9</sup> that it is more often seen than any other type. In the Central and Northern Provinces, the incidence of the disorder is less marked; and in Lower Bengal, where dysentery furnishes a larger contribution to the mortality returns than any other single disease, the amœbic variety appears to be comparatively rare.

Statements as to its frequency, however, vary considerably. Of seventeen patients in the Campbell and Police Hospitals at Calcutta, who were suffering from dysentery, ROGERS, in 1902, found<sup>10</sup> amœbic infection only in one; but his later work indicates that this was an exceptionally low proportion. VIERECK states<sup>11</sup> that, of twenty cases of amœbic dysentery treated at the Seamen's Hospital in Hamburg, the infection had been acquired at Calcutta in eleven instances, in two instances at other Indian ports, five times in China, once in Japan, and once in Cochin China.

In Rajputana and the drier parts of the Punjab and North-West Provinces, amœbic dysentery is infrequent,<sup>12</sup> but many cases have been reported from the upper Gangetic Provinces; and in the planting districts of Northern and Central Bengal it is undoubtedly very common.

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<sup>8</sup> C. F. Fearnside, "Dysentery in the Prisons of the Madras Presidency," *Indian Medical Gazette*, July, 1905.

<sup>9</sup> Powell, *British Medical Association Report*, 1908.

<sup>10</sup> L. Rogers, *Brit. Med. Journ.*, and various papers, 1902, 1903, 1905.

<sup>11</sup> H. Viereck, "Studien über die in Tropen erworbene Dysenterie" (Beihefte). Leipzig: J. A. Barth, 1908.

<sup>12</sup> A. Duncan, *Brit. Med. Journ.*, 1902, ii., 242.

Throughout Assam and Burmah the disease is endemic, and it appears to be equally prevalent in the seaports and country districts. In Dacca, Comilla, and Rajshahi, in Eastern Bengal, Major ANDERSON found amœbic organisms in 50 per cent. of all cases of dysentery, and identified the great majority of these as *Entamœba histolytica*.<sup>13</sup>

The high rate of mortality which prevails among the coolies employed in the tea gardens and plantations in Eastern Bengal is largely due to amœbic infection, introduced, in most cases, from Southern India. In Tenasserim, the Mergui Archipelago, and the Western Provinces of Siam, an acute form of dysentery is very prevalent; but a large number of cases which were examined there by the writer showed that the disorder was almost invariably of amœbic origin.

An interesting research also carried out by Major ANDERSON, at the penal settlement of Port Blair in the Andaman Islands, showed <sup>14</sup> that a very large proportion of the prisoners harboured intestinal Protozoa. During the year 1905, 2,539 cases of dysentery were admitted to hospital, and in 920 of these, special investigation as to the nature of the disease was instituted. In 455 cases amœbæ were found in combination with flagellates (*Trichomonas* and *Lamblia*), and in twenty-nine they were the only protozoan parasites; in four instances *Balantidium* was present in combination with flagellates and amœbæ, and once only was it found alone. Of 210 patients, not suffering from dysentery and admitted for other diseases, seven were shown to harbour intestinal amœbæ alone; fifty-four, amœbæ and flagellates; and eighty, flagellates alone. Thus, in only 167 out of 920 cases of dysentery could

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<sup>13</sup> Anderson, *Brit. Med. Journ.*, 1908, ii., 1244.

<sup>14</sup> Anderson, *Indian Medical Gazette*, April, 1907. *Idem*, *Brit. Med. Journ.*, 1908, ii., 1243.



none of these Protozoa be demonstrated; while less than a third of all the other patients were free from protozoan infection.

The type of dysentery is mild, for of 4,719 cases treated in 1904-5 only 298 were fatal; and as the patients, almost without exception, belonged to the criminal and poverty-stricken classes, this proportion indicates a non-malignant form of disease. Major ANDERSON'S statistics are, moreover, instructive, inasmuch as the convict population of the Andamans is representative of almost every race and province of the Indian Empire, and the ratio of infection of new arrivals may, therefore, be regarded as fairly reflecting the conditions which prevail throughout India.

In Ceylon, where dysentery of a malignant type is extremely prevalent, the amœbic variety of the disease is uncommon. CASTELLANI,<sup>15</sup> who examined the dejecta of 150 dysenteric cases in the Government hospitals, found entamœbæ in two only; and although one writer states<sup>16</sup> that amœbic dysentery is prevalent in the hill districts, amœbic infection appears to be comparatively rare. In both of CASTELLANI'S cases the disease was complicated by hepatic abscess, but in neither instance could entamœbæ be found in the pus. An additional point of interest in CASTELLANI'S report is that both patients were included in a series of twenty-three cases of dysentery in which a special bacteriological examination was carried out, and that neither showed a Shiga-Kruse infection, although the specific bacillus was successfully demonstrated in nineteen of the others.

No definite statistics as to the prevalence of amœbic dysentery in Asia Minor and Arabia are available, but infection is now known to be more general than has been supposed. The dysenteric

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<sup>15</sup> Castellani, *Journ. of Hygiene*, 1904, iv., 495.

<sup>16</sup> Fernando, *Brit. Med. Journ.*, 1905, i., 875.

diarrhœa by which pilgrims returning from Mecca are so frequently attacked, and which in Semitic countries sometimes assumes an epidemic form, is declared by Drs. RUFFER and ZIROLIA<sup>17</sup> of the International Sanitary Commission to be true amœbic dysentery. KARTULIS states<sup>18</sup> that the Hedjaz acts as the medium of distribution, and that the pilgrim-diarrhœa—so frequently seen at the quarantine stations of Egypt—is a typical example of the epidemic occurrence of the disease. The fact that an enormous number of pilgrims from infected countries annually flock to Mecca, where they live under most unhygienic conditions, sufficiently explains these outbreaks; but there is also good reason to believe that amœbic dysentery is endemic and very prevalent in the country itself.

Throughout tropical and subtropical Africa, amœbic dysentery is ubiquitous. It is exceptionally prevalent in alluvial districts along the courses of the great rivers, where floods are frequent, and where surface drainage is often defective. In Egypt the case-incidence of amœbic dysentery is higher, in proportion to population, than in any other country in the world; but the occurrence of the disease is limited almost entirely to the low-lying tracts of land adjacent to the Nile. On the other hand, in the oases and desert regions of Egypt amœbic infection is infrequent; but in parts of Tunis, Algiers, and Morocco<sup>19</sup> it appears to be very prevalent.

In South Africa, amœbic infection is uncommon on the dry uplands of the interior, although in the coast towns, and especially in the Portuguese and German<sup>20</sup> colonies, and in Natal, it is of

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<sup>17</sup> Zirolia, *Bulletin Quarantenaire*. Alexandria, June 9, 1904.

<sup>18</sup> Kartulis, Kolle and Wassermann's "Handbuch." Jena, 1907, p. 352.

<sup>19</sup> Marchoux, *Comptes rendus; Soc. Biol.*, 1899, p. 870.

<sup>20</sup> Hillebrecht, "Ueber Ruhr-artige in Deutsch. Sud-West Afrika," *Archiv. f. Schiffs und Tropen-Hygiene*, 1906.

frequent occurrence. The camp dysentery which proved so fatal in the Transvaal and Orange Free State during the war of 1901 was almost wholly of the bacillary type<sup>21</sup>; but fifteen out of the thirty-seven cases identified as amœbic dysentery in the Hamburg Seamen's Hospital were contracted in South African ports. According to RÜGE, it is endemic in Madagascar.

Throughout the equatorial provinces and in the Western Territories of Africa, acute dysentery, although by no means infrequent, is apparently less prevalent than in most other parts of the tropics. PROUT states<sup>22</sup> that in the Gold Coast Colony the commonest clinical variety of the disease is a subacute form of dysenteric diarrhœa, which is rarely fatal, but which shows a marked tendency to become chronic. Entamœbæ, however, can seldom be demonstrated, and hepatic abscess is rare.

In Senegal, on the other hand, MARCHOUX<sup>23</sup> reports that amœbic dysentery is endemic. At the Settlement of St. Louis, where the disorder is unusually prevalent, it frequently assumes an epidemic type; and, almost every year, during the months of July and August, the case incidence rises rapidly. In 1898, forty-seven cases, of which two were fatal, occurred in the French garrison. The principal clinical features of this outbreak of dysentery were mildness of type and protracted course, whilst the specific nature of the infection was clearly indicated by the fact that entamœbæ were found in the dejecta of every one of the patients. Hepatic abscess was, however, a rare complication.

Little exact information is available as to the prevalence of amœbic dysentery in other provinces of Central Africa, but the

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<sup>21</sup> Report of the Commission of Inquiry, South African War, 1903.

<sup>22</sup> *Transactions of the Society of Tropical Medicine and Hygiene*, 1908.

<sup>23</sup> Marchoux, "Note sur la dysenterie des pays chauds," *Comptes rendus Soc. Biol.*, 1899, 870.

disorder is stated to be moderately frequent in Lagos, in the Niger and Congo valleys and deltas, in Kamerun,<sup>24</sup> and throughout the lake regions in Uganda, and in the East Coast Protectorate. CREIGHTON WELLMAN has informed the writer that at Angola he repeatedly verified the existence of both types of dysentery, and that hepatic abscess is often seen as a sequela of the amœbic variety of the disease. A malignant form of epidemic dysentery—probably bacillary—is prevalent on the caravan routes, but it occurs only during the dry season. Amœbic dysentery is endemic in Benguela.

In the Western Hemisphere, relatively to latitude, amœbic dysentery is, perhaps, even more prevalent than it is in the Old World. Most of the tropical States of North and South America are endemic centres of the disease; whilst in the temperate regions of both continents it is also extensively disseminated. In the West Indies, although hepatic abscess is rare, the flux which is so prevalent and fatal throughout Central America has been shown to be mostly of amœbic origin. In the Panama Canal region, amœbic dysentery was formerly very prevalent<sup>25</sup>; whilst in Florida<sup>26</sup> and in Texas,<sup>27</sup> it is stated to be more common than any other variety of severe illness.

Throughout Brazil,<sup>28</sup> Venezuela, Chile, and the Amazon valley, amœbic dysentery is also very prevalent; but in Argentina and the other Southern Republics, although cases are occasionally recorded,<sup>29</sup>

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<sup>24</sup> A. Plehn, "Die Dysenterie in Kamerun," *Archiv. f. Schiffs und Tropen-Hygiene*, 1898, 125.

<sup>25</sup> Osler, *Medical News*, 1902, and other papers.

<sup>26</sup> Nasse, *Deutsch. med. Wochenschr.*, 1891, 881.

<sup>27</sup> Dock, *Texas Medical Journal*, 1891, 419.

<sup>28</sup> Fajardo and others, see *Centralbl. f. Bakt.*, 1896.

<sup>29</sup> Dessy and Marotta, "Sobre la existencia de la enteritis disenterica y del absceso del higado en Argentina," *Ann. Med. Circ.*, 1905.

it is infrequent. In the mortality returns published by the Government of Brazil,<sup>30</sup> a fatal issue is ascribed to amoebic dysentery once for every three times that the bacillary type is certified as the cause of death; and it is noteworthy that, in Rio de Janeiro at least, children and young adolescents appear to be affected much more frequently and severely than in other countries.<sup>31</sup>

In Polynesia and the tropical districts of Australia, amoebic dysentery is responsible for a large share of the excessive mortality from intestinal diseases which prevails throughout the whole of these regions. It has been repeatedly identified in Fiji; and a recent epidemic disorder which occurred in that colony was shown to be due to amoebic infection. Similar outbreaks appeared at the same time in several of the European stations of New Guinea and New Caledonia, and at the latter settlement the affection was conclusively proved to be true amoebic dysentery.

Although preferentially a tropical or subtropical disease, amoebic dysentery is not uncommon in cold countries, and it is widely distributed throughout the temperate zones of both hemispheres. It is endemic in many parts of Southern Europe, and is exceptionally prevalent in Italy, Sicily, Malta, and the Balkan Peninsula. KRUSE and PASQUALE observed numerous cases in Naples, Aquila, and Calabria; whilst CELLI and FIOCCA showed that Rome, Siena, Belluno, and Forli were deeply infected, and SCHAUDINN found it in abundance at Rovigno.

The occurrence of the disease is by no means limited to South Europe. It is not uncommon in Austria-Hungary,<sup>32</sup> Poland,

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<sup>30</sup> *Boletim Estatistica*. Rio, 1907.

<sup>31</sup> O. De Oliveira, "Dysenteria amebica na infancia," *Brazil Medicina*. Rio, 1904, 321.

<sup>32</sup> Hlava, *Centralbl. f. Bakt.* (Ungarn), i., 537.

Bavaria, and most of the Northern States of Germany.<sup>33</sup> In 1901,<sup>34</sup> amœbic dysentery appeared in epidemic form among troops stationed in East Prussia, and similar outbreaks have been noted<sup>35</sup> in garrison towns throughout Russia and Siberia. Numerous instances of purely indigenous origin have been seen in France and in England; and a careful study of a case of amœbic dysentery, followed by hepatic abscess, in a man who had always lived in Birmingham, appears<sup>36</sup> in a recent issue of the *British Medical Journal*.

A case lately described<sup>37</sup> by Messrs. CAUSSADE and JOLTRAIN before the Société des Hôpitaux in Paris, is so typical of amœbic infections as they are seen in Europe, that it appears to be worthy of citation. The patient was a man who had never been out of France, or, so far as he knew, in contact with anyone who had dysentery. He was attacked by diarrhœa, the dejecta soon becoming dysenteric in character. Subsequently, a hepatic abscess with a pulmonary vomica developed. No amœbæ could be found in the excreta, nor could dysentery bacilli be grown from them. The blood, moreover, did not agglutinate cultures of the Shiga-Kruse or Flexner bacillus, but there was marked eosinophilia. Amœbæ were ultimately found in the pus from the lung cavity, and at the autopsy, sections made from ulcers in the colon showed the amœbic infection to be severe and typical.

In no country have so many reports of cases been published as in the United States; and there can be no doubt that amœbic

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<sup>33</sup> Steffenhagen, "Amœbendysenterie mit sekundär Leber Abscess."

<sup>34</sup> Jägers, "Ueber Amœbenbefunde bei epidemischen Dysenterie," *Berl. klin. Wochenschr.*, 1901, xxxvi., 917.

<sup>35</sup> Voroshilski, *Protok. Omsk. Med.*, 1935.

<sup>36</sup> Saundby and Miller, *Brit. Med. Journ.*, March, 1909.

<sup>37</sup> *Lancet*, 1907, i., 694.



dysentery is much more prevalent in the temperate districts of America than in the isothermal zones of the Old World. Professor OSLER declares it to be by far the most common type of dysentery in that country, and he further states that at Baltimore the other varieties of the disease are seen but rarely. MUSSER,<sup>38</sup> of Philadelphia, says that the great prevalence of amœbic dysentery there is a conclusive argument against its being regarded as a tropical disease, or as having any special affinity for the tropics. DOCK<sup>39</sup> met numerous instances of amœbic dysentery in Georgia, but when he removed to Ann Arbor, in Michigan, he searched for amœbæ in vain. The occurrence of amœbic dysentery has recently been noted by NYDEGGER<sup>40</sup> at New York, by LAMB<sup>41</sup> at Washington, by BOGGS<sup>42</sup> in Virginia and other Southern States, by ELLIS<sup>43</sup> in Texas, by WAUGH<sup>44</sup> at Chattanooga, by TUTTLE<sup>45</sup> in Ohio, and by C. F. CRAIG,<sup>46</sup> FITZ and GERRY,<sup>47</sup> and many other writers in most of the Northern States of the Union.

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<sup>38</sup> Musser, *Brit. Med. Journ.*, 1902, ii., 242.

<sup>39</sup> Dock, *Medical Record*, July, 1891.

<sup>40</sup> J. A. Nydegger, *West Virginia Med. Journ.*, 1907, ii., p. 15.

<sup>41</sup> *Washington Medical Annual*, 1907.

<sup>42</sup> T. R. Boggs, *Virginia Med. Semi-Monthly*. Richmond: 1908.

<sup>43</sup> *Texas Cour. Record Medical*. Fort Worth: 1906, 7, xxiv., 1.

<sup>44</sup> Waugh, *Southern Med. and Surg. Journal*. Chattanooga: 1905.

<sup>45</sup> J. P. Tuttle, *Lancet Clinic*, Cincinnati, 1905; and *Jour. of the Amer. Med. Assoc.*, Chicago, 1904.

<sup>46</sup> C. F. Craig, "The Pathology of Chronic Specific Dysentery," *Journ. of the Assoc. of Military Surgeons*, 1904, &c.

<sup>47</sup> Fitz and Gerry, *Boston Med. and Surg. Journal*, 1891.





**PART II.--BIOLOGICAL.**



## CHAPTER IV.

CLASSIFICATION AND GENERAL RELATIONS OF PROTOZOA TO  
INTESTINAL DISEASES.

ALTHOUGH important information as to the life-history and pathological relations of the Protozoa has recently been acquired by the study of human and comparative parasitology, the zoological position of the group is still uncertain. From a medical point of view most of the illnesses which originate in infection by pathogenic Protozoa bear a close analogy to bacterial diseases, and if a classification on a clinical basis were possible, these organisms might reasonably be included in the vegetable world; but, so indefinite are the biological features dividing them from unicellular plants on the one hand, and from metazoan organisms on the other, that most zoologists regard Protozoa as distinct from both kingdoms, and consider their establishment as a separate Class to be essential to an exact appreciation of their place both in Medicine and Natural History.

In classifying primitive organisms it is now, however, usual to rely on the indications afforded by their habits of life rather than on morphological characters; and it is therefore generally agreed to accept Protozoa as a separate sub-kingdom of the animal world; their constitution being roughly defined by including within the group all organisms which, although consisting structurally of but a single cell, maintain an independent existence, and perform the functions usually associated with animal life.

The great majority of the Protozoa are free-living, and parasitism is the exception; but in each of the four orders into which the sub-kingdom is divided, viz. (1) Rhizopoda, (2) Sporozoa, (3) Flagellata, and (4) Infusoria, parasitic forms are found; and the second division, Sporozoa, belongs altogether to that category. From the standpoint of general pathology, also, the Sporozoa are of greatest importance, as the order includes most of those Protozoa which find their natural habitat in the circulation. The Rhizopoda, on the other hand, take first rank as intestinal parasites, in that they include the organisms which are responsible for the causation of amoebic dysentery; but numerous Sporozoans, Flagellates, and Infusorians are also found in the alimentary canal, and some of them have more or less well-defined pathogenic functions.

In the zoological scale the Rhizopoda are the lowest division of the sub-kingdom, and, regarded as animals, they are, perhaps, the simplest of all forms of life; for the complete organism consists of nothing more than an uncovered cell of protoplasm, which moves and encloses food particles by means of temporary extrusions of its own body substance. They are subdivided into a large number of sub-classes, orders, and genera; but most of them are free-living, and only one order—that of Amœbœa—comprises organisms which are parasitic in man.

The order Amœbœa is further divided into three genera, *Amœba*, *Chlamydomphrys*, and *Leydenia*—all of them parasitic. Of these, however, *Amœba* is alone worthy of special notice: for, of the other two—both of which contain but one species—*Leydenia* has been found only in the peritoneal fluid, and *Chlamydomphrys enchelys*, although its occurrence is not unusual in the human intestine, has no pathogenic function.

As to the further sub-division of the Amœbæ there is much difference of opinion, but the system which is now generally adopted

is that of SCHAUDINN. The classification, was not, however, originally made by that observer, for although it is known by his name, it is based on previous rearrangements of the genus by CASAGRANDE, BARBAGALLO, and JURGENS. In this scheme, the genus *Amæba* is divided into two sub-genera—viz., *Amæba* and *Entamæba*. The use of the former term to denote first a genus, and, again, a sub-genus of the order, is confusing, and the nomenclature will no doubt be altered; but in the meantime it stands, and is generally adopted by zoologists.

Of these subgenera, *Amæba* has many species, some of which are occasionally found as parasites of the digestive system and its accessory structures, but none of them possess any definite pathological importance. *Entamæba*, again, is subdivided into two species—*Entamæba histolytica*, the pathogenic organism of amœbic dysentery, and *Entamæba coli*, a harmless intestinal parasite.

## CHAPTER V.

## THE ENTAMŒBÆ OF THE HUMAN INTESTINAL TRACT.

*Technique and Methods of Demonstration.*

*Fresh Specimens.*—At all stages of the disease, the dejecta of a patient suffering from amœbic dysentery usually contain living entamœbæ; and if a drop of the excreted mucus is placed under a microscope, one or two organisms may generally be observed. As a rule they are easily seen; and, after a little experience, there is seldom any difficulty in determining, almost at once, whether a given specimen contains entamœbæ. Like other Protozoa, however, they are apt to be elusive, and for their successful demonstration certain precautions are necessary.

It not infrequently happens that in the portion of material which is subjected to examination, no entamœbæ can be discovered, although there may be considerable numbers of them in other parts of the stool; and care must be taken to secure a specimen in which organisms are likely to be found. The mucus passed as the result of straining usually contains entamœbæ; and they are almost invariably present in the gelatinous matter and flakes of disintegrating membrane which form the latter part of a dysenteric motion. There is no more likely situation than the edges of a small shred of sloughed mucosa; and, if it is taken from freshly passed excreta, placed with some of the mucus in which it is suspended on a slide, and quickly examined, specific entamœbæ will almost certainly be seen.

It is, further, important that nothing be allowed to interfere with the natural movements of the organisms. Their normal refractive index varies but little from that of thick mucus, and their outlines, in consequence, are sometimes almost invisible. In such cases, if not in motion, they are easily overlooked; but the characteristic changes of shape and position afford material aid in identification. Excreta intended for examination should, therefore, be preserved from contact with urine and disinfectants; and it is desirable that the patient should not have been recently treated by calomel or other intestinal antiseptics. In cold weather the receptacle should be warmed; and if that is done by boiling water accidental contamination by free-living amœbæ will at the same time be avoided. In the tropics, and in ordinary circumstances at home, a warm stage is unnecessary, for entamœbæ are usually quite active at a temperature of from  $15^{\circ}$  to  $20^{\circ}$  C.

A suitable fragment having been selected, it should be placed on the centre of a clean cover-glass. For this purpose a platinum loop is generally unsatisfactory; the exact particle which is wanted can seldom be picked up, and smooth blunt forceps, with a pair of scissors to divide strings of mucus, are more useful. The specimen may be examined as a film or in a hanging drop. If the former method is adopted the cover-glass is gently lowered on to a slide, and lightly pressed down; when a hanging drop is preferred, the edges of the cover are vaselined, and it is placed on a hollow-ground object-glass in the usual way. Should the mucus be exceptionally viscid, dilution with normal saline solution, slightly warmed, facilitates observation; as, apart from the fact that movements are then freer, the refraction of the medium corresponds less closely to that of entamœbæ.

The specimen should be examined with a full illumination, and in the first instance by a moderately low power. For making a



search a magnification of 80 to 100 diameters is most serviceable ; but in order to distinguish species, higher powers are desirable, while for detailed structural observation an immersion lens ( $\frac{1}{12}$ -in. or  $\frac{1}{16}$ -in.) is necessary.

In examining dysenteric dejecta, one of the first things to strike an observer is the fact that there is no definite relation between the severity of the symptoms and the number of organisms which are excreted ; often, in acute attacks, only one or two may be seen, while in mild cases they may be abundant. There is, besides, great irregularity in their frequency ; a copious infection may be noted at one time, and without obvious change in the condition of the patient or in the characters of the dejecta, organisms, at the next search, may be very rare.

*Fixing and Staining.*—For purposes of diagnosis stains are generally unnecessary and whenever possible, intestinal protozoa should be examined fresh. Apart from the aid to identification afforded by their movements, the organisms are often so contracted and altered by fixing and colouring processes, that they present but a faint resemblance to their natural appearance, and definite information as to their life processes can only be gained by the study of fresh specimens.

Both *Entamœba histolytica* and *E. coli*, however, stain readily with most of the aniline dyes, and assistance in distinguishing them rapidly from each other, and from other cells in fresh dejecta, may be obtained by adding a small quantity of weak aqueous solution of acid fuchsin to the specimen. By this method, detritus and epithelial cells are coloured red, whilst the entamœbæ are left almost unstained ; they are, however, much shrunk and altered in appearance by the action of the reagent.

For permanent preparations, one of the simplest and best methods is to fix a film on a slide by gently rubbing a small piece

of slough or mucus on the glass, which, when dried in the air, is placed in the vapour of osmic acid for twenty minutes, and afterwards washed with tapwater. Another well-known method of fixing entamœbæ is the process recommended by SCHAUDINN. After spreading and drying a film on a cover-glass, it is floated (preparation down) in a watch-glass containing a mixture of two parts of saturated watery solution of perchloride of mercury with one part of absolute alcohol. The fixative is then heated to 70° or 80° C., over wire gauze, for ten minutes, at the end of which time the film is washed in 70 per cent. alcohol, flushed with water, and dried.

The ordinary fluid fixatives, such as the solutions of ORTH, FLEMMING, and HEIDENHAIN, alcohol, chromic acid, &c., should not be employed for films or streak preparations of entamœbæ, as they distort the organisms and often render them quite unrecognizable. Fixing fluids, however, act well when the entamœbæ are in the tissues, and sections of intestine which have been hardened in HEIDENHAIN'S mercuric salt solution, or in MÜLLER'S fluid concentrated in an incubator for three days, give satisfactory views of the organisms *in situ*.

Specimens so fixed may be stained in various ways. A simple method is to dip the film for one minute in a 50 per cent. solution of tincture of iodine, afterwards clearing by washing it in 90 per cent. alcohol. Although they take the colour slowly, entamœbæ may also be well stained by hæmatoxylin and eosin. Solutions of hæmatin in alcohol, and of alum in the proportions recommended by DANIELS,<sup>1</sup> having been matured and tested, a small quantity of the unfiltered stain is placed on the film for ten minutes, at the end of which time it is flushed off, and the specimen is dried after

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<sup>1</sup> C. W. Daniels, "Studies in Laboratory Work." London, 1903, p. 53.

washing in tapwater. The film may then be counterstained by placing it in a 1 per cent. solution of eosin for half a minute, after which, it is finally washed and dried.

HEIDENHAIN'S iron hæmatoxylin process<sup>2</sup> is one of the best general stains for intestinal Protozoa, and MALLORY'S modification<sup>3</sup> of his technique is simple and effective. Nigrosin also secures good definition of structure, and has been much employed by German observers, many of whom regard this stain as more permanent and suitable for this class of work than any other.

For differential chromatin colouring, ROMANOWSKY'S process is generally advisable, and the best specimens of entamœbæ, both in film and in tissue, may be obtained by Giemsa's effective modification of that stain. In this method, Giemsa's fluid (Grubler) is slowly added to distilled water until the translucency of the mixture is approximately that of dark port wine, and the film or section is at once immersed in the solution. The specimen must remain in contact with the dye for twenty-four hours, after which time it may be dried, washed, and mounted.

Many of the stains in ordinary use lack permanency; and a specimen of entamœbæ, especially when mounted in Canada balsam, is often quite invisible in less than a month. Films show less tendency to fade when put up without a cover-glass, and if kept dry will last indefinitely. The best specimens, too, are secured by light staining; for structural detail can be seen clearly only when the organisms are faintly coloured. In fæcal films, moreover, bacteria are sometimes excessively numerous, and when deeply stained they may obscure everything else. Bacteria-free films may sometimes be obtained from hepatic abscesses.

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<sup>2</sup> For particulars of the application of this process, see a paper by Captain Hamerton, "Methods of Study," &c., *Journ. Royal Army Medical Corps*, 1908.

<sup>3</sup> Mallory and Wright, "Pathological Technique," 1901, p. 397.

When *E. histolytica* is stained lightly in Giemsa, the homogeneous ectoplasm remains almost uncoloured and appears as a clearly differentiated, slightly tinted area, whilst the granular endoplasm assumes a deeper blue shade. The scanty chromatin of the nucleus, if at all visible, is seen as minute scarlet points or fibrils, and the ingested blood corpuscles are pale pink. The whole of the body substance of *E. coli*, when subjected to the same process, stains dark blue, the outer zones being, however, somewhat fainter in colour. The nucleus, on account of the abundance of its chromatin, shows numerous deep purple-red fibrils and spots.

## CHAPTER VI.

THE ENTAMŒBÆ OF THE HUMAN ALIMENTARY TRACT—  
MORPHOLOGY AND STRUCTURAL COMPARISON.

ENTAMŒBA HISTOLYTICA.—In the living condition, the pathogenic agent of dysentery assumes an endless variety of form. When at rest it tends to become globular, and is seen as an irregularly shaped spherical or ovoid mass ; but, on account of almost incessant motion in the cell protoplasm, the appearance is continually changing. With the commencement of movement, the organism elongates in one direction, becoming pear-, sausage-, or kidney-shaped ; but after further extrusion of pseudopodia from the circumference, irregularity becomes still more marked, and, in its active state, the amœba appears as a multiform body of infinite diversity and complexity of outline.

Similar movements are common to most rhizopoda, although in *E. histolytica* structural peculiarities in the formation of the pseudopodia are distinctive of the species ; and, in the cell itself, the following specific characteristics may generally be readily identified :—

(a) A clear homogeneous field of jelly-like protoplasm, usually known as ectoplasm, which, when the organism is at rest, occupies about a third of the whole area.

(b) A roughly granular endoplasm, which constitutes the remaining two-thirds of the total contents.

(c) A faintly defined nucleus and nucleolus.

(*d*) Inclusions of blood corpuscles, bacteria, and food particles.

The cell-organism itself is enclosed by a thin line of tissue, which is, however, almost imperceptible where the granular endoplasm reaches the margin, and is well-defined only at the periphery of the homogeneous field. Even there it cannot be identified as a definite membrane, for no characteristic structure can be distinguished; and it varies in clearness with the specific gravity of its surroundings. In a thick medium, which presumably approximates to the density of the clear zone, the line is hazy and indistinct; but in thin fluid, or in normal saline solution, it stands out with sharp definition. Further, as granules and other objects readily pass out and in at all points of the periphery, and as the organism is known to contain no cellulose, it is practically certain that the body substance is not enclosed by a true cell-wall, and that the line which is seen is merely the limit of the protoplasm rendered perceptible by difference of refraction.

The **HOMOGENEOUS TRANSPARENT PROTOPLASM**, or **ECTOPLASM**, is generally described as forming a complete zone round the granular endoplasm, but during life that distribution is of very rare occurrence. It varies in size and position with the condition of the organism, and, in ordinary circumstances, the so-called ectoplasm is situated at one or both ends of the cell. When pseudopodia are thrown out, hyaline protoplasm invariably collects behind the periphery at the point where the extrusion is taking place, and there is always, therefore, a clear field at the anterior pole of the entamœba, in the direction in which movement is taking place.

The arrangement of the ectoplasm is, in consequence of that disposition, segmental rather than circumferential, and the granular endoplasm is usually in direct contact with the periphery at one or more places. In these situations no clear area can be seen to intervene between it and the edge of the cell; and, except that the



ectoplasm is never enclosed by granular matter, nor completely cut off from the periphery, it has little claim to its title.

The area which the ectoplasm occupies also varies with the digestive activity of the organism. When food particles are englobed by the entamœba, they are thrust at once into the granular matter, which may thus become so distended as to fill up the whole of the body space, the homogeneous area being pushed aside, and compressed until it becomes almost invisible. With the absorption of the nutritious matter and the expulsion of refuse, the hyaline protoplasm appears to expand, until, in the fasting condition, it again occupies half or one-third of the organism.

Although no structure can be made out, and although neither vacuoles nor food particles can be seen in the homogeneous protoplasm, there is no doubt that it is, nevertheless, strictly specialized in composition as well as in function. The highly refractive appearance suggests that it is of infinitely greater tenacity and hardness than the rest of the cell; and the disposition indicates that it subserves the purposes of motion and prehension rather than those of digestion. It is, moreover, definitely connected with the pathogenic function of the species; for it is by means of the long and sharp pseudopodia of hyaline material that *E. histolytica* is able to thrust itself between the cells of epithelial and glandular structures, and to tear asunder the connective tissue fibres.

THE GRANULAR PROTOPLASM varies considerably in appearance and opacity. In some specimens it is pale and finely granulated, and, not infrequently, its limits can be differentiated from those of the homogeneous protoplasm only by a slightly deeper shading. In the majority of cases, however, it is coarse, densely opaque, and sharply separated from the hyaline protoplasm; and it is often so closely packed with clumps of granules that the nucleus and included bodies which it contains are quite invisible.



It is difficult to explain these variations, for, even under the highest powers of the microscope, the granular protoplasm appears to be structureless; no fibrillar tissue, nor any appearance suggestive of an areolar network, can be distinguished. The colour varies with the food which has been ingested, and with the number of granules; but, in ordinary circumstances, the endoplasm of *E. histolytica* has a pale, greenish-yellow tint—that of *E. coli* being brownish-grey—and the general formation is that of a thick gelatinous fluid, in which particles of granular matter are embedded.

The granular endoplasm is also much less viscid than the homogeneous ectoplasm, for distinct currents and streams may often be seen in it, and Harris states that motile bacilli which have been ingested continue to move about freely. There can be no doubt that it is contractile and resilient; and its capacity for varied and rapid movement is shown not only in locomotion, but by the way in which food particles are thrust deeply into the interior, and their *débris* afterwards expelled from the periphery. The granular endoplasm also possesses marked assimilative functions, and it is able to deal with an astonishing quantity of food.

ENTAMŒBA COLI.—In *E. coli* there is no separation of granular from hyaline area. Granular protoplasm fills the whole of the organism; and although here also there is sometimes a little variation in the intensity of the shading, no distinction can be drawn between the protoplasm of which the pseudopodia are formed and the rest of the cell contents. When locomotion takes place, the absence of the clear field at the anterior pole is especially noticeable; and this marked characteristic is one of the most important indications in the identification of species. A transparent ectoplasm is, practically, peculiar to *E. histolytica*, and the formation of hard and powerful pseudopodia differentiates that

organism from *E. coli* and from all other cells that are found in the intestinal contents.<sup>1</sup>

Another notable point of distinction between *E. histolytica* and *E. coli* is that the granular endoplasm of the former almost

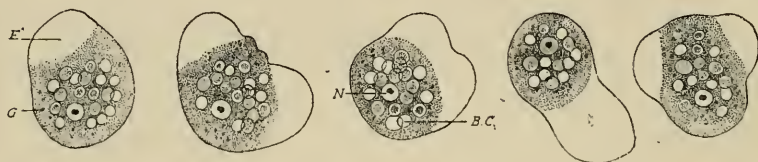


FIG. 1.—*Entamoeba histolytica*.  $\times 375$  (semi-diagrammatic). *E*, Ectoplasm or hyaline protoplasm; *G*, granular endoplasm; *N*, nucleus and nucleolus; *B.C.*, ingested blood corpuscles. (The nucleus is placed more centrally, and is larger and more distinct than it usually appears.)

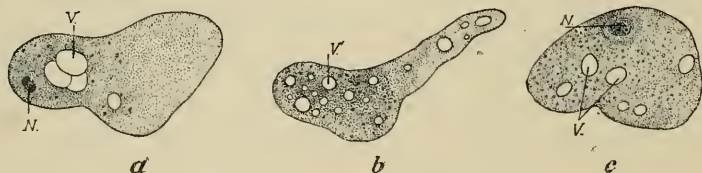


FIG. 2.—*Entamoeba coli*.  $\times 500$  (semi-diagrammatic). *a*, Commencing movement; *b*, in motion (nucleus obscured); *c*, at rest; *N*, nucleus; *V*, vacuoles.

invariably contains considerable quantities of ingested blood. It is by no means unusual to find twenty or thirty englobed corpuscles in one organism; and in many cases the whole of the interior is closely packed with these cells. Ingested blood corpuscles are never

<sup>1</sup> Prowazek states that *Amœba buccalis* also possesses a hyaline ectoplasm, but that it is distinguished from *E. histolytica* by its nucleus, which is central, and more defined. (*Arbeiten aus dem Kaiserlichen Gesundheitsamte Leitseite*, xxi., 42.)

seen in *E. coli*; but the vacuoles, which are of common occurrence in the endoplasm of that species, must be carefully distinguished from blood cells.

In other respects, the protoplasm of *E. coli* differs but little from the granular endoplasm of *E. histolytica*. It is, however, somewhat finer and lighter in texture and the granules are smaller.

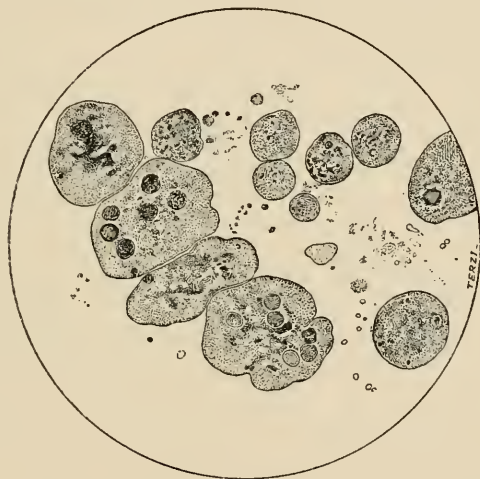


FIG. 3.—*Entamoeba histolytica*. Organisms in dysenteric mucus.  $\times 400$ . The granular protoplasm occupies almost the entire cell, and is distinguished from the ectoplasm only by a slight difference in shading.

In both species the endoplasm generally contains numerous minute fragments of solid matter—apparently foodstuff and bacteria. The structural granules themselves are derived from two sources; they may be nuclear, that is to say, they may be fragments of chromatin extruded from the nucleus, or they may be metaplastic—residue from the digestion of food. The former resemble shreds of a fibrillar structure; the latter are more angular,

and look like grains of pigment. These varieties of granules are easily distinguished from each other.

The process by which blood corpuscles are ingested by *E. histolytica*, and their ultimate fate after being included in the endoplasm of that organism, are imperfectly understood; for although living entamœbæ have been watched for long periods in fluid media in which blood cells were plentiful, and to which fresh blood was from time to time supplied, and although the conditions were as nearly as possible normal, the actual enclosure of a red blood corpuscle by an organism has never been observed. So far at least as specimens of entamœba which are under the microscope are concerned, it is, moreover, very doubtful whether any absorption takes place; and, as it is certain that there is no expulsion of residue, many observers have claimed that the process has no place in the nutrition of the organism.

It can scarcely be doubted, however, that blood corpuscles are captured by entamœbæ in the same way that bacteria and smaller particles are englobed by leucocytes, and that they are afterwards assimilated by a process akin to phagocytosis. Digestion seems to be temporarily arrested when the organism is placed in the light, but the appearances are so distinctive as to leave little room for any other conclusion.

In both varieties of entamœba a nucleus may be seen; but there are marked differences in its position and structural arrangement in the respective species.

In *E. histolytica*, the nucleus, although a constant structure, is generally ill-defined, easily mistaken for an ingested blood corpuscle, and often very difficult of identification. It is about 4 to 6  $\mu$  in diameter, ovoid or elongated in shape, and it is generally placed eccentrically to the granular protoplasm, lying almost on the periphery of that substance. It contains very little chromatin,

and, in consequence, stains badly, no definite nuclear structure, filaments, or chromidia being apparent. A small bladder-like nucleolus, in which lies a grain of pigment, is always present. When the endoplasm is opaque, and crowded with granules, blood corpuscles, or other ingested matter, the nucleus may be completely obscured, but the addition of dilute acetic acid to the specimen generally brings it into view.

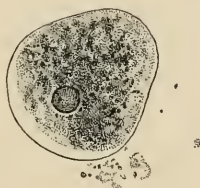


FIG. 4.—*Entamoeba histolytica*.  $\times 500$ . Fixed in osmic acid vapour, and stained by safranin. (After Jürgens.) The nucleus and nucleolus are slightly coloured. There are no freshly ingested corpuscles, but the granular endoplasm contains *débris* and matter suggestive of the remains of blood cells. The hyaline ectoplasm is well seen.

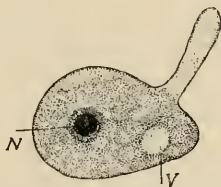


FIG. 5.—*Entamoeba coli*.  $\times 500$ . Fixed, while in motion, by osmic acid vapour and stained with safranin. The nucleus, which is rich in chromatin and has a shaded areola, is well seen. V, vacuole.

In *E. coli* the nucleus is generally deeply placed in the interior of the endoplasm. It is clearly defined, and, in most cases, easily seen; in shape it is spherical, and apparently vesicular, and it is separated from the endoplasm by a line, usually of remarkable sharp-

ness, and by a definite areola. Unlike the nucleus of *E. histolytica*, it contains a large quantity of chromatin, and it stains deeply with any nuclear stain. A small nucleolus may sometimes be seen.

The presence of VACUOLES is an important feature in the differentiation of species. Briefly stated, the distinction is that *E. histolytica* contains blood cells and no vacuoles; and that *E. coli* contains vacuoles and no blood corpuscles. Round, transparent, faintly coloured discs, from 3 to 5  $\mu$  in diameter, are not infrequently observed in the interior of *E. histolytica*, and they are often described as cavities in the granular matter. The nature of these bodies is, however, doubtful; the general appearance and a characteristic yellowish tint suggest that they may be partially digested blood corpuscles; but, if that is so, it is difficult to explain why, although considerably smaller than red cells, they are always uniform in size. They have, however, nothing in common with protoplasmic vacuolation, for they can be seen to react to pressure and to the influence of movement in exactly the same way as semi-solid structures.

In *E. coli* several well-developed vacuoles can generally be seen, but their presence is not invariable. They vary greatly in size and in distribution, and they are usually scattered all through the protoplasm, two or three large ones being often grouped near the nucleus. They are easily obliterated by pressure.

*Size of Intestinal Entamœbæ.*—*E. histolytica* is usually described as being considerably larger than *E. coli*; and difference of size is regarded by many writers as an important specific distinction. In neither species, however, is size a constant character, and it is, therefore, of little diagnostic value. The usual diameter of *E. histolytica* is from 20 to 30  $\mu$ , and specimens measuring 40  $\mu$  are by no means rare; but, on the other hand, undoubted examples no more than 10 to 12  $\mu$  in breadth are frequently seen.



It is also the case that, in different patients and in different attacks of amœbic dysentery, the specific organisms vary considerably in size. In some infections they are almost all large, in others almost all small; and although no relation has been shown to exist between size and the severity of the seizure, it is probable that different "strains" of *E. histolytica* vary in virulence as they do in bulk. Apparent size is, moreover, influenced by different conditions, and especially by the density of the surrounding fluid. In the same way that the periphery becomes more clearly defined in a thin fluid, the whole entamœba appears to increase in size after the addition of normal saline to the medium in which it is living.

*E. coli* usually measures from 12 to 25  $\mu$  in diameter, and as it very rarely exceeds the latter figure, the statement that the organism is smaller than *E. histolytica* is so far correct.

*Movement and Locomotion.*—In favourable conditions entamœbæ are seldom or never at rest; and when not in active movement from one place to another, alterations in their outline and in the arrangement of the endoplasm are continually taking place. The manner in which these changes in shape and position are effected is, moreover, characteristic of the species; and valuable aid in the distinction of *E. histolytica* from *E. coli* is afforded by observation of the movements and by the conformation of the pseudopodia.

If a living specimen of *E. histolytica* is watched for some time, it will be seen that at some particular point the periphery bulges, and that hyaline protoplasm collects under the protuberance. This swelling subsides almost as soon as it forms, but immediately reappears in another segment of the circumference, the process being repeated again and again almost without intermission. It may also be observed that these continuous movements, though apparently confined to the ectoplasm, begin in the centre of the organism, and



that they are invariably preceded by a change in the granular protoplasm. The first indication of commencing motion is that the granules, nucleus, and foreign bodies in that substance are momentarily swayed backwards and forwards as if by a current of liquid protoplasm. Movement towards one point of the periphery ultimately predominates, and the subsequent change in outline takes place at that spot ; but the granular protoplasm does not reach the periphery, and a thick cushion of hyaline matter always intervenes between it and the protuberance which is formed.

In both species locomotion is effected merely by an extension of the pseudopodia in one direction. In *E. coli*, the gray protrusion which is pushed out from one pole of the elongated organism becomes longer and larger, the body protoplasm flowing in until nothing is left behind. In *E. histolytica* the pale-coloured pseudopodia appear at first structureless, glassy and homogeneous ; and for an appreciable time after their formation they are without granular endoplasm. Ultimately, however, that substance pours steadily into their interior until the whole of the organism is gradually transferred into what was once only a protrusion of hyaline ectoplasm.

The pseudopodia of *E. histolytica* are generally somewhat thicker and stouter than the finger-shaped protrusions of *E. coli*, although this is by no means a distinctive characteristic. The ends of the projections in both species are rounded and sometimes club-shaped ; but those of *E. coli* are soft and flaccid, whilst the terminal extremities of *E. histolytica* appear horny and resistant, their formation and movements suggesting great tenacity and strength.

In a thin fluid locomotion is, naturally, more active than in dense surroundings, but the rapidity with which *E. histolytica* moves through a tenacious medium, and the ease with which it can push aside obstructions, are very remarkable. The movements of *E. coli*,

on the other hand, are limited in scope and lacking in vigour, and outside the body they quickly fail and cease.

When entamœbæ are in motion a considerable quantity of *débris* adheres to the back part of the organism, and as in *E. histolytica* the granular endoplasm collects in the posterior end, it is often very difficult to determine whether the matter is really adherent, or whether some of the protoplasm is not escaping.



FIG. 6.—*Entamoeba histolytica*. Dying and dead forms. In some the clear ectoplasm and the nucleus can still be seen; in others, structural disintegration has already set in. "Mulberry" knobs well shown.  $\times 400$ . (After Kartulis.)

*Death of the Organism.*—The duration of life is unknown. When conditions are favourable, as in the alimentary canal, both species undoubtedly live for a considerable time—probably for some weeks, or for one or even two months—but, outside the body, even although a suitable temperature and other essential conditions are maintained, vitality soon begins to fail. *E. histolytica*

is much more tenacious of life than *E. coli*; the latter dies almost at once, but, on a stage with a regulated temperature, the former sometimes lives for three or four days.

After death, both species contract in size and assume a spherical shape. In *E. histolytica* the granular endoplasm becomes lighter and less opaque; the nucleus takes up a more central position, and, in consequence of increased transparency, both it and the nucleolus can generally be easily made out (see fig. 4). This clear structural definition is, however, of short duration, for within twenty-four hours decomposition sets in, and soon afterwards nothing can be seen but a granular mass.

At death, *E. coli* also becomes paler, the change in shade being especially noticeable near the periphery, and suggesting the formation of a separate ectoplasm.

When death takes place suddenly, it is often preceded by violent agitation of the endoplasm and spasmodic movements of the whole organism. Short, irregular, and malformed pseudopodia are thrust out at various points of the periphery, and these extrusions sometimes persist as rounded mulberry-like knobs on dead entamœbæ of both species.

*Distinction of Entamœbæ from other Objects.*—Free-living amœbæ, leucocytes, and epithelial or other organic cells may be readily mistaken for entamœbæ. The contamination of faecal matter by free-living amœbæ after it has been selected for examination is by no means rare. In the Tropics especially, there is often abundant opportunity for the development of these organisms in the water which is used to clean vessels and receptacles, and unless care is employed they may easily find their way into specimens selected for examination. The resemblance between entamœbæ and many free-living species is, moreover, sometimes very close, and it is to be noted, as VIERECK points out, that several of the latter have resting stages which can scarcely be distinguished from those of parasitic forms.

As a rule, free-living amœbæ can be recognized by the fact that almost all of them are furnished with a pulsating or contractile vacuole. This, however, is not an absolute characteristic, for several free-living amœbæ have been described which have no contractile vacuole ; but, so far as is known, that structure is never seen in parasitic entamœbæ ; and if in dysenteric dejecta an organism is found in which there is a contractile vacuole, it may safely be regarded as a result of accidental contamination.

From large leucocytes entamœbæ may usually be differentiated by their greater size, by the characteristic formation of their pseudopodia (especially noticeable in *E. histolytica*), and by their wider activity and freedom of movement.

It happens, not infrequently, that, as a result of catarrhal inflammation of the colon, an extensive desquamation of the epithelial layers takes places, and that numerous degenerating cells are shed into the intestinal contents. Many of them are water-logged and swollen, and in this condition they sometimes present a superficial resemblance to entamœbæ. Observation, however, reveals almost complete lack of structure and general disintegration ; and, apart from these differences, epithelial cells are easily distinguished from living entamœbæ by the fact that they exhibit no change of outline or position.

## CHAPTER VII.

THE ENTAMŒBÆ OF THE HUMAN ALIMENTARY TRACT—  
REPRODUCTION.

SO far, the examination of the intestinal entamœbæ presents no serious obstacle, and the morphological characters which differentiate species may generally be identified during the routine observation of a case of amœbic dysentery. The methods by which the organisms multiply, although still more distinctive of species, are on the other hand exceedingly complex and difficult to follow, so much so that for clinical purposes they are practically unavailable. Their importance, however, is so great that a brief statement of the prominent features in the processes of reproduction is necessary.

Our knowledge of the reproductive stages, and especially of the sexual multiplication of intestinal entamœbæ, is almost entirely due to the researches of SCHAUDINN.<sup>1</sup> He showed that in the case of *E. histolytica* the facts are as follow:—

Multiplication may occur during the active life of the organism within the intestine, in which case it is generally, if not always, asexual. This sometimes takes the form of binary fission, that is to say, the whole entamœba after cleavage of the nucleus divides into two equal parts; but more often asexual multiplication is effected by means of budding. In the latter case, after dispersion of the nuclear contents in the endoplasm, an indefinite number of

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<sup>1</sup> F. Schaudinn, *Arbeiten aus dem Kaiserlichen Gesundheitsamte*, 1903.

daughter entamœbæ, each containing fragmentary chromatin, are irregularly extruded from the periphery of the parent organism, to which, however, they remain joined by a narrow neck. A nucleus having been formed by the collection of the included chromosomes, this attachment ruptures and the young entamœbæ are set free. These processes correspond to the schizogony of other protozoa.

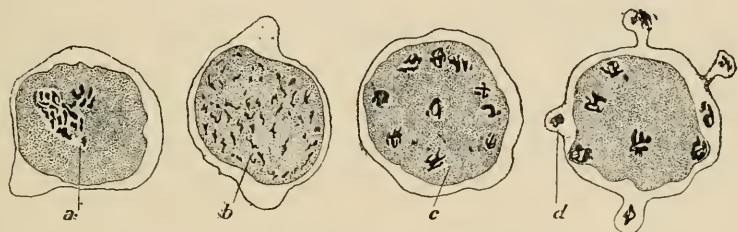


FIG. 7.—*Entamoeba histolytica*. Asexual multiplication by budding.  $\times 900$ . *a*, *b*, Dispersion of nuclear contents in the granular endoplasm; *c*, collection of chromatin for the nuclei of the young entamœbæ; *d*, formation of buds. (After Schaudinn.)

More frequently, however, multiplication takes place by spore formation or sporogony. At a certain period in the life of the organism it becomes mature, and it then enters on a resting or quiescent stage of existence. SCHAUDINN states that he is entirely unable to trace the influences that determine maturity in any species of amœba; but the condition should be distinguished from the formation of resistant cysts, which is induced by unfavourable external conditions. In the latter state *E. histolytica* is usually seen as a spherical body, 10 to 20  $\mu$  in diameter, with a clearly defined envelope. The cell contents are of a uniform pale grey colour, and present no appearance of structure. No nucleus is visible. In the sexually mature organism, the division between



hyaline and granular protoplasm is readily distinguishable, and the nucleus is easily seen.

After a special form of nuclear division and subsequent conjugation, most of the indistinct chromatin of the nucleus is shed into the endoplasm; the nucleus consequently degenerates, and the residue is expelled. The fragments of chromatin afterwards collect at various points of the periphery, and form themselves into an uncertain number of minute spherical cysts, each 3 to 7  $\mu$  in diameter, by the aid of a filamentous membrane derived from the hyaline ectoplasm. These small bodies subsequently separate from the organism and form resistant spores which are able, probably after passing through another phase, to develop into new individuals. The parent entamœba thereupon rapidly degenerates and dies.



FIG. 8.—*Entamoeba coli*. Asexual multiplication by binary fission.  $\times 900$ . (After Craig.)

In comparison with these progresses, and with the indefinite formation and number of buds and spore-cysts in *E. histolytica*, the reproduction of *E. coli* is more typical and regular. In this species, multiplication by schizogony, which also occurs only during the intra-intestinal life of the organism, may take the form either of binary fission or of a special type of multiple division. In the first process, there is no diffusion of the chromatin through the cell protoplasm, and the nucleus simply splits up into two halves. When nuclear separation is almost complete, the cell protoplasm constricts, opposite the point of separation, and the organism divides into two equal segments.



When schizogony by multiple fission takes place, the nuclear chromosomes, after dispersion through the body substance, collect at eight separate and almost equally distributed points to form the

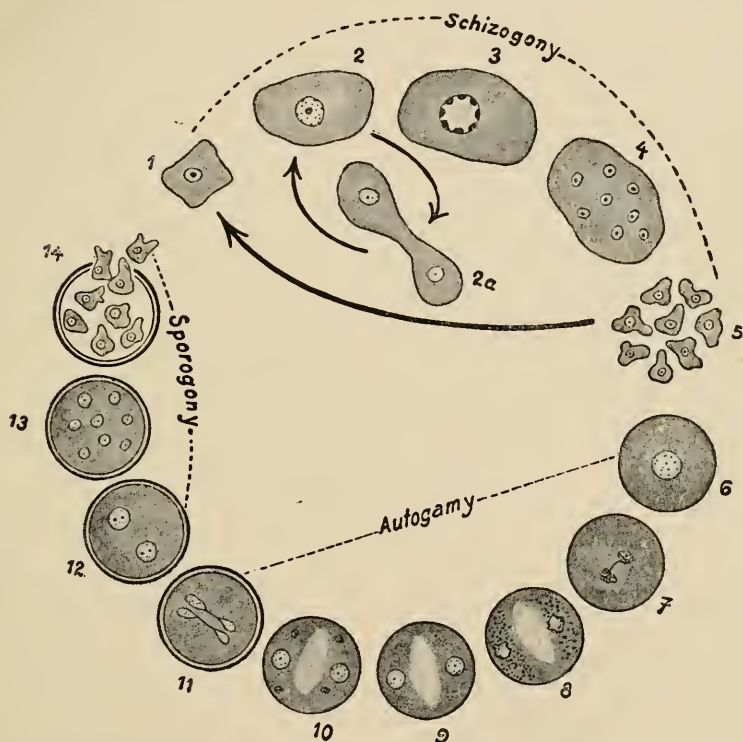


FIG. 9.—*Entamoeba coli*. Schematic representation of asexual and sexual reproduction. (1) Young organism; (2 and 2a) binary fission of mature cell; (3, 4, 5) multiple fission; (6) encysted entamoeba; (7, 8, 9) nuclear re-arrangement and division; (9, 10, 11) secondary cleavage and reunion of chromosomes; (12, 13, 14) formation of zygote-nucleus and spores.

nuclei of the new organisms. These minute filaments of chromatin then arrange themselves as a delicate fibrillar network, and each group becomes invested by a definite membrane, which appears to

be developed from the cellular protoplasm. The nuclear structure being thus complete, the parent entamœba breaks up into eight daughter amœbulæ, which disperse in the intestinal contents and rapidly grow to their full size.

Sexual reproduction, or sporogony, in *E. coli* takes place when active life ceases, and the organism arrives at maturity. At this stage, encystment always occurs, but the process differs from the reproductive encystment of *E. histolytica* in that it is certainly hastened, if not invariably produced, by unfavourable conditions. The gradual solidification of the intestinal contents in their downward passage is adverse to the continuance of active life; and, when found in solid dejecta, *E. coli* is never in the active, but always in the encysted condition. In this respect, it offers a marked contrast to *E. histolytica*, which, under similar conditions, is generally active for at least one or two days.

No difference, however, can be observed between mature and immature cyst formation, and sporogony apparently follows the latter process in exactly the same way as it does the former. With encystment, *E. coli* reaches the so-called stage of reconstitution. In this condition, the organism assumes a perfectly globular form; granules, bacteria, and other foreign bodies are expelled from its interior; the endoplasm becomes absolutely transparent; a soft, gelatinous membrane forms on the surface, and the nucleus divides into two halves which recede to opposite poles of the cyst. On account of the extreme clearness of the protoplasm at this stage, the changes in the nucleus are easily seen, and Schaudinn stated that in spite of the complexity of the processes of sexual reproduction, he knew of no cell more suitable for nuclear study than the encysted stage of *E. coli*.

The divisions of the nucleus, after reconstruction of their own nuclear arrangement, subsequent reduction of chromosomes, and

increase in the thickness of their cyst-walls, again divide into two halves, of which one persists as a clear shining globule, and the other further subdivides into two bodies of similar size, but of a dull appearance. These results of nuclear division and reconstruction now enter on the stage of copulation, during which, by means of a spindle-shaped arrangement of chromosomes, the elements traceable to one source of origin approach and finally coalesce with those of an opposite derivation. As an effect of this complicated but not unusual protozoan form of sexual union, a double nucleus—known as the zygote-nucleus—ultimately appears; and this reconstituted body ultimately splits up into eight smaller nuclei. Here, again, adherence to the type number of eight is apparently constant.

After this final division the young broods of nuclei develop coverings of protoplasm and form colonies of eight minute amœbulæ within the old envelopes. To effect their release the cyst must be swallowed by a new host, and when that occurs the envelopes are dissolved and the enclosed amœbulæ are set free to commence independent life in the upper tract of the alimentary canal.

Craig states<sup>2</sup> that he has observed simple conjugation in both species of entamœbæ. The process consists in the fusion of apparently similar organisms, with subsequent blending of the nuclei. As yet, however, this important observation has not been fully confirmed.

For comparative table of differences *see* next page.

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<sup>2</sup> C. F. Craig, "International Clinics," Philadelphia, vol. iii., 1907.

COMPARATIVE TABLE OF CHARACTERISTIC DIFFERENCES BETWEEN  
ENTAMŒBA HISTOLYTICA AND ENTAMŒBA COLI.

	<i>E. histolytica</i>	<i>E. coli</i>
Size ...	Not a reliable characteristic; but generally 20—30 $\mu$ , often smaller	Diameter 12 to 25 $\mu$ . Size also not absolute in this species.
Colour ...	Generally greenish ...	Generally brownish grey.
Ectoplasm ...	Hyaline, and clearly differentiated from the granular endoplasm.	No differentiation of hyaline protoplasm from endoplasm.
Granular protoplasm	Nothing characteristic in structure or appearance. It generally occupies about two-thirds of the body space.	Nothing characteristic in appearance, it fills the whole of the body space.
Pseudopodia ...	Thick and stout. Formed first by hyaline protoplasm; hard and horny. Movements powerful and apparently purposed.	Finer and more finger-shaped. Are of the same substance as the endoplasm. No preliminary inflow of hyaline protoplasm; they appear soft and flaccid.
Nucleus ...	Generally eccentric in position; elongated or oval in shape; indistinct and often invisible; deficient in chromatin.	Generally sub-central in position; clearly-defined, vesicular, spherical, separated from endoplasm by a line of remarkable definition and a clear areola. Contains much chromatin.
Cystic condition	A spherical body with clearly differentiated envelope and uniform pale grey structureless conformation of cell contents.	Very clear and translucent, the surface covered by a transparent gelatinous membrane; nucleus easily seen.
Vacuoles ...	None. ...	Two or more, but vacuolation not invariable.
Reproduction	(1) Asexual, by binary fission or by budding.  (2) Sexual, by spore cysts, which form resistant spores.	(1) Asexual: (a) by binary fission; (b) by formation of eight daughter-cells. (2) Sexual. After reconstitution and nuclear changes by formation of a zygote nucleus, which divides into eight smaller nuclei and amœbulæ.

## CHAPTER VIII.

THE ENTAMOEBAE OF THE HUMAN ALIMENTARY TRACT—  
CULTIVATION.

THE cultivation of Amœbæ has naturally engaged much attention, and innumerable experiments have been undertaken to determine the practicability and utility of their artificial growth. So far as the free-living species are concerned there is no difficulty; they are ubiquitous, and grow in, or on, any medium to which they can accommodate their requirements. But it is otherwise with the parasitic varieties; and the most that can be said at present is that some of them appear to have been successfully cultivated. Several authorities, indeed, question the reliability of the whole of the experiments which have been made with the human entamœbæ, and especially with *E. coli*, and roundly assert that, so far, the latter organism has never yet been reproduced in artificial culture.

It is undoubtedly true that most of the early cultivation experiments, such as those of CUNNINGHAM,<sup>1</sup> GRASSI,<sup>2</sup> and VIVALDI,<sup>3</sup> are now completely discredited. These observers claimed that they had been able to cultivate *Amœba coli* from dysenteric dejecta, and that the cultures, when introduced into the lower intestines of cats, set up dysenteric symptoms; but subsequent research has shown that

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<sup>1</sup> Cunningham, Annual Report of the Sanitary Commissioners, India, 1870.

<sup>2</sup> Grassi, "Dei protozoi parassiti," *Gaz. Med. Ital.*, 1879.

<sup>3</sup> Vivaldi, "Le amebe della dissenteria," *Riforma Med.*, 1894.

the organisms with which they were working were free-living species which had accidentally contaminated the media.

The later researches of LEIDY,<sup>4</sup> MONTI,<sup>5</sup> OGATA,<sup>6</sup> BEYERINCK,<sup>7</sup> and FRÖSCH,<sup>8</sup> are somewhat more reliable. Working on continuous lines, they were able to show that, provided the reaction of the medium was slightly alkaline, and that great care was exercised in the maintenance of a suitable temperature, many parasitic Rhizopoda and Infusorians would reproduce and develop on various solid and liquid substances. FRÖSCH also made the important observation that symbiosis with some variety of bacterium was in many cases an essential condition of growth.

In 1898 TSUJITANI gave further prominence to the theory of symbiosis by reporting<sup>9</sup> that, although he had been unable to grow parasitic amœbæ in pure culture on a freshly-prepared medium, he had effected their development by planting encysted forms in media on which pathogenic bacteria, when growing, had previously been killed by heat.

Subsequent investigations lent additional support to the view that bacterial life is necessary to the growth of entamœbæ. In their report,<sup>10</sup> MUSGRAVE and CLEGG corroborated and extended Tsujitani's results. They agreed that parasitic varieties could not be grown alone in pure culture; but in symbiosis with different species of bacteria, some of which were strongly preferential, they were able to cultivate intestinal amœbæ. On a medium of bouillon

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<sup>4</sup> Leidy, *Proc. of the Acad. of Nat. Sci.*, Philadelphia, 1874, 1877.

<sup>5</sup> Monti, "Cultiv. d. Amœbe," *Boll. Sci.*, Pavia, 1895.

<sup>6</sup> Ogata, "Ueber die rein Kultur gewisser Protozoen," *Centralbl. f. Bakt.*, 1893.

<sup>7</sup> Beyerinck, "Culturversuche d. Amöben," *Centralbl. f. Bakt.*, 1896.

<sup>8</sup> Frösch, "Zur Frage d. Reinzucht v. Amöben," *Centralbl. f. Bakt.*, 1897.

<sup>9</sup> Tsujitani, "Ueber die Reincultur der Amöben," *Centralbl. f. Bakt.*, 1898.

<sup>10</sup> Musgrave and Clegg, "Amebas: their Cultivation and Etiologic Significance," Manila, *Reports of the Biological Laboratories*, 1904.



and agar, one per cent. alkaline to phenolphthalein, to which a trace of peptone had been added, they found that the organisms developed freely at room temperature if some form of bacterial life were added to the culture; and they further showed that, as a commensal, the spirillum of Asiatic cholera suited intestinal amœbæ better than any other.

Their method of segregation was ingenious; the dysenteric material was spread out on a sterile plate, and an isolated amœba was located by means of an AA Zeiss objective. When the organism had been carefully centred, a clean objective of DD magnification was substituted for the weaker power, and was then carefully lowered on to the amœba. In this way, the organism generally adhered to the lens, and could be transferred to a fresh plate, on which it developed in what they believed to be a normal manner when in combination with a bacterium.

MUSGRAVE and CLEGG'S observations are not altogether conclusive. The indications as to the species of organism with which they were working are somewhat indefinite. They did not accept SCHAUDINN'S classification—then recently published—and their descriptions of the adult forms of the amœbæ obtained by culture from dysenteric mucus almost lead one to the belief that, in some of their experiments at least, the organisms which they cultivated were non-parasitic varieties. On the other hand, in several of their illustrations, exact reproductions of the encysted stages of *E. histolytica* are to be found.

A further element of doubt arises from the circumstance that young cats, when experimentally inoculated with the cultures, remained quite well; although in a small percentage of cases monkeys, similarly infected, developed dysenteric symptoms, and amœbæ were found in their dejecta. A search for the symbiotic bacterium failed to reveal its presence in either case. As monkeys



are generally more resistant to artificial amœbic infection than cats, and as it is by no means unusual for them to acquire the disease naturally when kept in confinement, the evidence of successful culture supplied by these experiments is also open to question.

In the following year, A. LESAGE<sup>11</sup> published an important paper, in which he stated his conviction that *E. coli* had never been successfully cultivated either pure or in symbiosis; but that in seven out of thirty attempts he had succeeded, both at Saigon and at Toulon, in growing a parasitic amœba from mucous matter voided by patients suffering from tropical dysentery, and that he had no doubt that it was *E. histolytica*.

Two methods were employed. In the first, several specimens of mucus were removed from the dejecta, and placed for some hours in sterilized Petri dishes, the presence of living entamœbæ being verified in each instance. Small portions of mucus were then selected and transferred to sterile plates covered with gelatine which had been washed during eight days in running water. On a medium so prepared, it was found that entamœbæ developed freely at a temperature of 18° to 25° C., that the growth of the non-symbiotic intestinal bacteria was to a great extent inhibited, and that the more completely this was effected the more satisfactory was the culture of the protozoa. LESAGE also grew entamœbæ in symbiosis with innocuous bacteria; for this purpose, he found a species of *B. paracoli* specially useful; and he further showed that, cultivated in this way, the organisms developed directly by schizogony, and that they did not pass through a stage of encystment.

His second method was devised to obtain development by

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<sup>11</sup> Lesage, "Culture de l'amibe de la dysenterie des pays chauds," *Ann. de l'Inst. Pasteur*, 1905.

sporogony ; in other words, by culture of the living entamœba from its encysted stage. To effect this a small quantity of dysenteric mucus was spread round the inside of a sterilized and closely-covered vessel, shaped like a wine-glass, in the bottom of which was placed a little sterilized water. After slowly drying for several days in a moist atmosphere at  $18^{\circ}$  to  $25^{\circ}$  C., minute portions of the dried mucus, with some of the fluid from the bottom of the glass, were transferred to plates of washed gelatine and incubated at the same temperature.

In this way, although most of the encysted organisms perished or failed to develop, growths of entamœbæ were obtained in one out of every ten inoculated plates ; and, by successive sub-cultures, non-symbiotic bacteria were gradually eliminated. Some particular bacterial micro-organism was, however, always essential, but if that was supplied, there was no difficulty in continuing combined propagation. LESAGE states that during a period of two years he carried a growth of *E. histolytica* through a series of no less than sixty-six sub-cultures, in symbiosis with a bacterium. His method was to place the entamœbæ at the bottom of a plate of gelatine held vertically, and to inoculate the upper part with the bacterium ; after incubation for several days at  $25^{\circ}$  C., the growth of the entamœbæ extended until it reached the bacterium, and a fresh portion was selected to be again transferred to the bottom of another plate of gelatine.

His description of the morphology and biological relations of the organisms leaves little room for doubt that LESAGE did, in this manner, actually succeed in effecting artificial development of *E. histolytica*, but his experiments do not seem to have been carried to their necessary conclusion. He does not record that any attempt was made to communicate amœbic dysentery to animals, either by feeding or by rectal injection of cultures ; and without reproduction

of the disease, cultivation experiments, however successful, possess little practical value.

E. L. WALKER, of Harvard University, who has also cultivated intestinal amœbæ,<sup>12</sup> gives a general confirmation to the statements of previous observers. As a result of a very large number of culture experiments he arrives at the following conclusions:—

(1) Parasitic amœbæ grow only on the surface of a solid medium.

(2) They multiply only on a neutral or alkaline medium, not on one that is acid.

(3) The presence of living bacteria, on which the amœbæ probably feed, is an essential factor in cultivation.

(4) A free supply of moisture and free oxygen is necessary.

(5) The most suitable temperature is 20° to 25° C.

He thinks that, if these conditions are satisfied, the nutrient content and general composition of the medium have little, if any, influence on development.

WALKER further considers that comparison of various culture forms of amœbæ tends to discredit the accuracy of SCHAUDINN's classification. In this contention, however, his own observations do not support him. He was unable to cultivate amœbæ from dysenteric mucus, and the only type of pathogenic organism at his disposal was a specimen of *E. histolytica*, isolated from dysenteric material by MUSGRAVE and passed through several sub-cultures. As CRAIG<sup>13</sup> points out, the probability of contamination seriously depreciates the importance of these experiments.

On specially prepared nutritive media (potato, macaroni in

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<sup>12</sup> Walker, E. L., "The Parasitic Amœbæ of the Intestinal Tract of Man and other Animals," *The Journal of Medical Research*, February, 1908.

<sup>13</sup> Craig, C. F., "Studies upon the Amœbæ in the Intestine of Man." Chicago, 1908.

bouillon, gelatine), and in association with the bacillus of rat-typhus, A. GAUDUCHEAU has carried the cultivation of intestinal amœbæ a step farther.<sup>14</sup> The cultures were made directly from dysenteric material, and, although in certain of the younger specimens a pulsating vacuole was seen, there can be no question of the affinity, in other respects, of most of the organisms to *E. histolytica*. Both in the disposition of the ectoplasm and endoplasm, and in the general morphological characters of the organisms, the similarity of structural detail is very striking, whilst, by making use of SCHAUDINN'S method of fixation (corrosive sublimate and alcohol), GAUDUCHEAU was able to show that there are at least two distinct stages of development.

In the first, the organisms are no larger than  $8\mu$  to  $15\mu$  in diameter, and are spherical or ovoid in shape. Observed at this stage the nucleus is more distinct; it is generally central, surrounded by a clear space, and it contains a single karyosome, the adhesion of which to the nuclear periphery, with subsequent extrusion of chromatin, can be easily followed. Active reproduction takes place by budding, as well as by simple fission. In the later stage, the nucleus is eccentric, but the nuclear sac is somewhat more distinct, and the spherical karyosome is centrally placed. At this period, the organisms are difficult to keep alive, and with the exhaustion of the nutriment in the culture medium they degenerate rapidly. The decay, which is no doubt premature and a result of artificial growth, causes them to contract so much that their transverse diameter seldom exceeds  $1\mu$ ; even in pure culture the shrunken forms are difficult to see, and in the intestinal contents, presuming that they undergo a similar change, organisms of this size would be quite unrecognizable.

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<sup>14</sup> A. Gauducheu, *Bull. de la Soc. de Pathol. exot.*, 1909 (May 12 and July 21).

GAUDUCHEAU made the important observation that rabbits which had been treated by peritoneal injections of the cultures were rendered immune to experimental amœbic infection; and he was also able to show that it was by the development in the blood serum of qualities antagonistic to the growth of entamœbæ that this immunity was produced. In the diluted blood serum of control animals the organisms maintained their full vitality, but in the serum of immunized rabbits they quickly became motionless and ultimately encysted.

In Cochín China, NOC has recently cultivated a species of entamœba from cysts which he found in the contents of liver abscesses,<sup>15</sup> in dysenteric dejecta, and in the public water supply of Saigon. In many respects, the organism closely resembles *E. histolytica*, and is, apparently, pathogenic, but on account of an unusual degree of polymorphism, NOC is inclined to regard it as a new species.

The general result of these investigations indicates that, although considerable progress has been made in cultivation experiments, further research in this direction is necessary to confirm the accuracy of most of the conclusions, to elucidate the life-history, and to establish the exact pathological relations of parasitic protozoa. So far, indeed, the whole subject of cultivation is still in an unsatisfactory and unsettled condition.

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<sup>15</sup> Noc, *Ann. de l'Inst. Pasteur*, 1909, No. 3, p. 177.

## CHAPTER IX.

## OTHER PROTOZOAN INFECTIONS OF THE HUMAN ALIMENTARY TRACT.

BESIDES the entamœbæ, various other protozoa are parasitic in the alimentary canal, and several of them have been associated with definite manifestations of intestinal disorder. None of the human species are, however, very important; in most cases, the affections to which they give rise are comparatively trivial, and the symptoms, except in the single instance of Balantidian dysentery, indicate rather a reaction to mechanical irritation than a specific infection.

There is, moreover, much uncertainty about the life-history of most of these parasites, and our acquaintance with their extra-corporeal phases, and their reproductive cycles, is very imperfect; but of recent years there have been numerous reports of protozoan organisms being found in the dejecta in various forms of tropical flux; and it is probable that these infections are increasing in frequency, or, at least, that they are more common than was formerly believed to be the case.

RHIZOPODA.—In addition to *E. histolytica*, pathogenic functions have also been ascribed to several other varieties of the same genus; and HARTMANN has recently reported<sup>1</sup> a protozoan—which he claims to be a distinct species of entamœba—as being associated with a form of African dysentery. The individuality of

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<sup>1</sup> Hartmann: *Archiv. f. Schiffs- und Tropen-Hygiene*, vol. xii., 1908.



this organism, named by him *E. tetragena vel Africana*, has been corroborated by other observers, but its distinction from *E. histolytica* cannot be regarded as finally established. As in the case of NOC's entamœba, it is possible that the only variation is unusual polymorphism—a phenomenon which is not uncommon in some of the entamœbæ parasitic in the lower vertebrates.<sup>2</sup>

Among other varieties of amœba occasionally found in the alimentary tract may be noted *Amœba gingivalis*, which was dis-

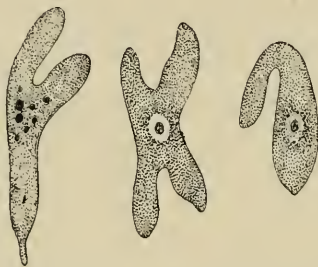


FIG. 10.—*Amœba gingivalis*. × 550. Living forms in motion.

covered in 1869 by GROS, and was afterwards demonstrated by FLEXNER, of Baltimore, in the pus of a maxillary abscess. It seems to be identical with the organism described by STERNBERG as *A. buccalis*, and by GRASSI as *A. dentalis* or *A. kartulisii*; and is notable, principally, because its spore-formation, as described by PROWAZEK, closely resembles the sporogony which SCHAUDINN observed in *E. histolytica*. It lives on the bacteria which flourish in the tartar of the teeth, and in the crevices and clefts of carious

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<sup>2</sup> See Clifford Dobell: "*Entamœba ranarum*." *Quarterly Journal of Microscopical Science*, 1909, No. 210.



cavities; but, although of fairly common occurrence, it has, probably, no pathogenic function.

Another intestinal amoeba, first described<sup>3</sup> by CASTELLANI in 1905, and named by him *A. undulans*, has a peculiar interest in that it suggests a possible relationship to the flagellate class of protozoa. About 30  $\mu$  in diameter, it extrudes only a single pseudopodium, and it is furnished with an undulating membrane. It was found in dysenteric dejecta; but, so far, this organism does not appear to have been again identified.



FIG. 11.—*Leydenia gemmipara*.  $\times 750$ . (After Schaudinn.) (a) At rest; (b) in motion; N, nucleus; V, protoplasmic vacuoles.

Besides entamoeba, two other genera of the order *Amæba*—*Chlamydomphrys* and *Leydenia*—are occasionally parasitic in the human alimentary canal. From a pathological point of view, these rhizopods are of little importance; the former—*Chlamydomphrys enchelys*—regarded by some zoologists as a foraminifer, is more frequently found in mammals and the lower vertebrates than in man; and, although specimens have been observed in dysenteric dejecta, blood corpuscles have not been seen in the protoplasm, and the organism appears to be otherwise innocuous.

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<sup>3</sup> A. Castellani. "Some Researches on the Etiology of Dysentery in Ceylon," *Journal of Hygiene*, 1904, p. 495.

*Leydenia gemmipara* was first discovered by LEYDEN, of Berlin, in the fluid of peritoneal ascites, but it has since been observed inside the bowel and in association with dysenteric symptoms. It increases rapidly by budding, the new individuals forming colonies by the intermingling of their long, thin pseudopodia; and the organisms are then seen as plaques of considerable size and unmistakable appearance.

**SPOROZOA.**—The Sporozoa are mostly intracellular blood parasites; and, although a frequent cause of fatal dysenteric epidemics in rodents and other animals, they rarely affect the human alimentary canal. Two intestinal species, however, *Coccidium cuniculi* (RIVOLTA), and *C. hominis* (EIMER), have been observed in man; and it is important to remember that these may occasionally be found in the dejecta when searching for amœbæ. Coccidia may be recognized by their large size, by their oval shape, and by the fact that they have at one extremity a minute depression—the micropyle. *C. cuniculi* measures from 40 to 50  $\mu$ , in its long, and from 22 to 28  $\mu$  in its short diameter; *C. hominis* from 25 to 30 by 15 to 20  $\mu$ .

Another species—*C. bigeminum*—originally described by WARDELL STILES as parasitic in some of the domestic animals, has recently been found by KJELBERG, of Berlin, in the epithelium of the human intestine.<sup>4</sup>

**FLAGELLATA.**—Although few of the flagellates are intestinal parasites, they have a very wide distribution, and are unusually prevalent in the Eastern tropics, where they are frequently found in the excreta of patients suffering from dysentery and diarrhœa.

*Lamblia intestinalis* is the commonest intestinal flagellate, and the most characteristic in appearance. The body is from 10 to

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<sup>4</sup> For an account of these Sporozoan parasites, see Blanchard: "Les Coccidies et leur rôle pathogène"—*Causeries scientifiques*.

16  $\mu$  in length, and from 5 to 10  $\mu$  in breadth; one shoulder being, as it were, cut away to form a sucker or adherent surface, by means of which the minute organism attaches itself to the free end of a single columnar intestinal cell. The favourite situation is the upper part of the ileum. There are eight flagella, six around the sucker and two at the posterior or free extremity. A nucleus and nucleolus are generally visible.

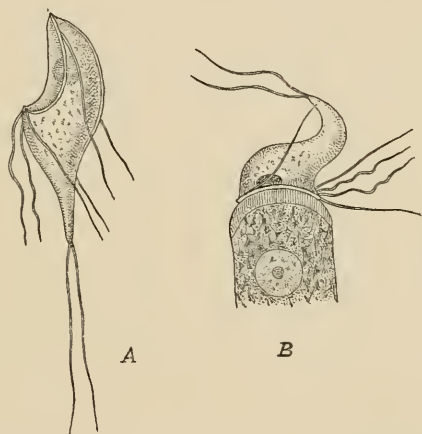


FIG. 12.—*Lamblia intestinalis*.  $\times 550$ . A, Free organism (side view); B, attached to an epithelial cell on an intestinal villus.

It is uncertain whether the organism has any definite pathogenic function, but, although frequently seen in individuals who are perfectly healthy, an abundant infection of *Lamblia* is usually attended by an irritative diarrhoea of persistent character and considerable severity. The cells to which it adheres are, moreover, quickly destroyed; and, as one organism attacks many cells in succession, extensive epithelial destruction is almost invariable. The method of infection is unknown; but it is probable that reproduction takes

place by means of encysted forms, and that they, or their enclosed spores, may be conveyed to food by mice or rats, animals which frequently harbour these parasites.

Several different species of the genus *Spirochæta* are also parasitic in the human intestine; and it is believed by many authorities that these flagellates are the specific causes of disorders which are variously described as spirillar dysentery, spirillar enteritis, diarrhée à spirochætes, spirillosis intestinalis, &c. Little, however, is known about spirochæte infections of the intestine. In the tropics, at least, spirillar organisms are often present in great numbers, although the abdominal functions are unimpaired; but, on the other hand, they are still more frequently found in the dejecta of patients who are suffering from intestinal complaints. Spirochætes are especially abundant in cases of infantile diarrhœa in the tropics.

There can be little doubt that in various morbid conditions spirochætes find the surface of inflamed mucous membranes highly favourable to their growth, and that they multiply with extraordinary rapidity; but no fatal case of spirillar diarrhœa has been described, nor do any definite *post-mortem* reports appear to have been published. The pathology of the condition is, indeed, very doubtful, and it is questionable whether any ætiological function can be ascribed to the organisms.

INFUSORIA.—Only a very few of the Infusorians are parasitic in man; but, of those which have been described, all are denizens of the alimentary tract. The most important is *Balantidium coli*, which is now regarded as the specific cause of the affection known as Balantidian dysentery.

*B. coli* is a frequent parasite in the lower part of the intestinal canal of many mammals, and is especially common in pigs. Man, although probably not a natural host, is also often affected; in the

Eastern tropics, Chinese, who eat large quantities of pork, harbour the parasites in enormous numbers; but the infection is by no means confined to warm countries, and it appears to be exceptionally prevalent in some parts of Russia, Poland, and South Germany. Balantidian dysentery is occasionally seen in England, where the fact that most of the cases occur in pork-butchers and others whose work brings them into frequent contact with pigs, indicates that the usual method of communication is by direct transmission of the parasite, or its ova, from animal to man. There are many circumstantial data in support of this view, not the least important being that in the tropics, at least, Jews and Mahommedans are never affected.

*Balantidium coli* is the largest of the protozoan parasites of the human alimentary tract. It is oviform in shape, bluntly pointed at one end, and it measures about  $\frac{1}{2}$  of a millimetre in length, and 50 to 70  $\mu$  in its short diameter. The organisms are, therefore, visible to the naked eye, and may often be seen quite plainly in the mucus of the lower intestine. The pellicle, or envelope, is a thin layer of almost transparent protoplasm marked by longitudinal striations, in the grooves of which lines of vibratile cilia are thickly planted. These appendages are chiefly locomotor in function; but, round the peristome, they are much longer, and are otherwise modified to assist in the capture of food particles.

The mouth, which is only a *cul-de-sac*, and not a true opening, is situated almost midway on the ventral surface at the termination of a funnel-shaped groove—the peristome—which begins at the rounded margin of the anterior end. The inside of the organism is closely packed with granular protoplasm, in which two, and occasionally three, slowly contracting vacuoles may be seen. Near the anterior pole there is a pale and homogeneous, but clearly defined, nucleus not unlike a malarial crescent in shape, and close



FIG. 13.—*Balantidium coli*. *a*, Natural condition ; *b*, reproduction by binary fission ; *c*, reproduction by sexual conjugation.

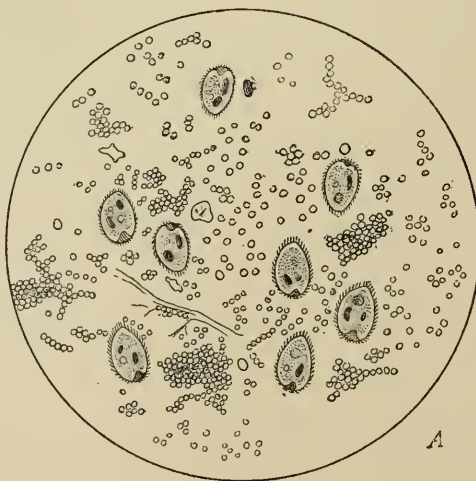


FIG. 14.—*Balantidium coli*. Living forms in the dejecta of Balantidian dysentery.



to it a micro-nucleus may often be seen. Reproduction, which takes place in the intestine, is generally effected by binary fission, but, sometimes, there is true sexual conjugation. In unfavourable conditions of life, such as it is likely to meet when expelled from the intestine, and possibly also as a normal stage of sexual reproduction, *Balantidium* encysts and forms minute sporocytes of exceptional vitality and tenacity. These are doubtless the medium by which, in ordinary circumstances, infection is conveyed from host to host.

Although, both in man and animals, *Balantidium* may undoubtedly be present in considerable numbers without detriment to health, there is strong evidence for the association of this parasite with a diseased condition of the lower bowel. The clinical manifestations are generally suggestive of proctitis or sigmoiditis; but, in many cases, the attacks are attended by dysenteric symptoms of considerable severity, and, not infrequently, they prove fatal. Over 120 cases of true Balantidian dysentery have been fully reported by different observers.<sup>5</sup>

*Balantidium* is seldom found in association with other intestinal parasites, and the invariable absence of entamoebæ and other rhizopoda when *Balantidium* is present in the alimentary canal is one of the most remarkable features of the infection.

The penetration of the intestinal walls by the parasite is difficult to demonstrate, for, with loss of vitality in the tissues of its host

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<sup>5</sup> For literature of Balantidian dysentery, see P. J. Wising, *Nord. Med. Arch.*, 1871; R. Blanchard, "Zoologie Médicale," 1889; O. Weit, *Deutsch. Archiv. f. klin. Med.*, 1898, p. 363; Solovieff, *Vratch.*, St. Petersburg, 1899, p. 1031; Strong and Musgrave, *Johns Hopkins Bulletin*, 1901, 12, 13; Solovieff, *Centralblat. f. Bakt. Parasitenkunde, &c.*, 1909, 29, 821; Askanazy, *Wiener med. Wochenschr.*, 1903, No. 3; Ehrenroth, *Zeitschr. f. klin. Med.*, 1903, 322; Klimenko, *Zeigler's Beiträge z. Anat. und Path.*, 1903; R. Strong, *Philippine Journ. of Sci.*, 1904; Dopter, *Archives de med. exp. et d'anatom. path.*, 1907, June, July and Sept.; Bowman, *The Philippine Journal of Science*, Dec., 1909.



*Balantidium* quickly perishes and disappears. Specimens of intestine intended for examination must therefore be cut and fixed immediately after death. Unless this precaution is observed, nothing will be seen ; but, if investigated at once, large numbers of

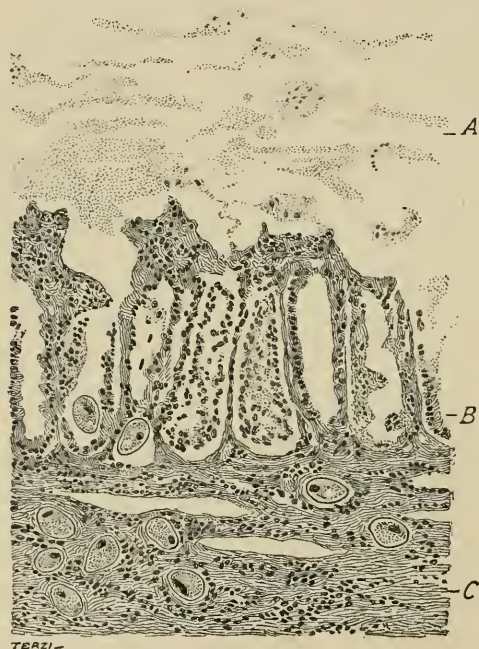


FIG. 15.—*Balantidium coli*. Invasion of the wall of the sigmoid flexure in a case of Balantidian dysentery. *A*, Mucus ; *B*, glandular infiltration and destruction ; *C*, parasites in the connective tissue of the submucosa, with infiltration of small cells. (After Dopter.)

parasites may generally be found in the glairy mucus which covers the inflamed mucosa, in the periglandular connective tissue, and in the vessels. Unlike entamoeba, *Balantidium* is seldom seen on the raw surfaces or bases of intestinal ulcers, the favourite position

being deep in the submucosa, where its invasion is followed by an abundant infiltration of small cells. It has frequently been reported as an intravascular parasite, and there is evidence that it may reach the liver and other organs through the lymph vessels (fig. 16). In

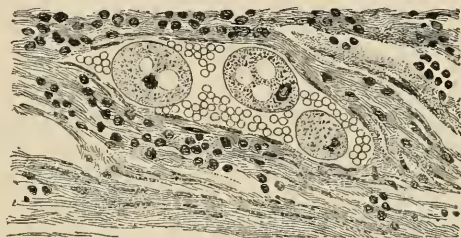


FIG. 16.—*Balantidium coli*. Parasites in a lymph space of the submucosa. (After Dopter.)

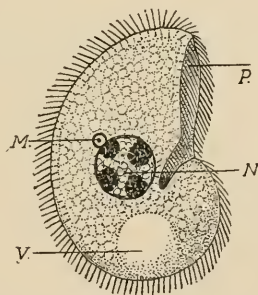


FIG. 17.—*Balantidium minutum*. P, Peristome; N, nucleus; M, micro-nucleus; V, vacuole. (After Schaudinn.)

Balantidian infections, necrotic areas and abscesses produced by embolisms of the parasite are frequently found in the liver, and occasionally in the spleen and lungs. *Balantidium* has, moreover, been observed in pus from a hepatic abscess which was expectorated through a pulmonary sinus.

A smaller *Balantidium*—regarded by SCHAUDINN as a separate species on account of its proportionately longer peristome—and named by him *Balantidium minutum*, has also been noted as a pathogenic variety. It closely resembles *B. coli*, but is only one-fourth or one-fifth of its size (20 to 30  $\mu$  by 14 to 20  $\mu$ ).

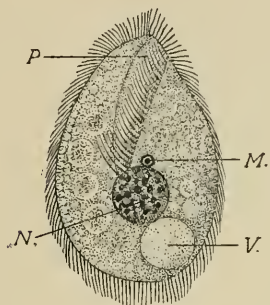


FIG. 18.—*Nyctotherus faba*. Showing peristome, nucleus, micro-nucleus, and food vacuole. (After Schaudinn.)

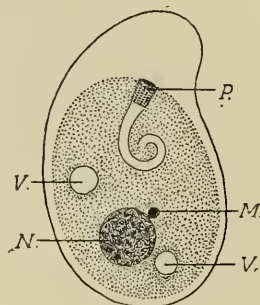


FIG. 19.—*Chilodon dentatus*. Showing similar structures, but different formation of peristome. (After Guiart and Guimbert.)

Other parasitic infusoria of still rarer occurrence in the human intestine, which have been definitely associated with dysentery, are *Nyctotherus faba*, slightly smaller than the last; *N. africanus*, found by CASTELLANI, at Colombo, in a negro suffering from trypanosomiasis with dysenteric symptoms, somewhat larger (40 to 50  $\mu$  by 35 to 40  $\mu$ ); and *Chilodon dentatus*, an abundant infection of which was observed by GUIART, at Paris, in the dejecta of a patient suffering from chronic dysentery.

**PART III.—CLINICAL.**



## CHAPTER X.

### THE SYMPTOMS OF AMŒBIC DYSENTERY.

ALTHOUGH constant in its tendency to chronicity, amœbic dysentery is essentially a disease of an irregular clinical type ; and there are wide variations in the intensity of the first attack as well as in the severity of the general symptoms. In some cases, the progress of the disorder is manifested by a series of intestinal derangements so insignificant in character that the patient is never confined to bed, and an advanced stage is reached before he is seriously ill. In the majority of instances, the infection is one of moderate severity, and the period of invasion is marked by acute dysenteric symptoms which gradually become less urgent, and ultimately assume a chronic and recurrent form. Occasionally, but rarely, the type is malignant ; when the patient, if he survives the first seizure, remains seriously ill, and succumbs during a relapse of acute dysentery.

The ONSET of amœbic dysentery, in some 60 per cent. of all cases, is acute. After an incubation period of from three to five days, during which there is persistent malaise and headache, these symptoms increase in severity, and the patient suffers from intense nausea which is only partially relieved by vomiting. In most cases there is also, at this time, a continuous sense of cold or chill ; and not infrequently the illness commences with a sharp rigor. Soon afterwards, spasms of griping pain, followed by frequent loose motions, are felt in the abdomen. At first, the pain is intermittent

and acute, and is most severe in the umbilical region ; but it afterwards becomes dull and continuous, and is then referred to the sigmoid area. It is usually described as a dragging and burning sensation in front of the sacrum, with intermittent sharp twinges which shoot down and through the rectum.

The dejecta are at first loose and watery, and contain considerable quantities of fæcal matter. At this stage the symptoms closely resemble those of ordinary irritative diarrhœa ; there is excessive intestinal discomfort ; calls to stool are urgent, and defæcation is attended by scalding and tenesmus. With the progress of the attack, the motions assume a dysenteric type. They are passed more frequently, and straining and pain increase with each movement of the bowels. The voided matter is no longer copious and fæcal ; after the first few motions it becomes scanty, and consists almost entirely of mucus, blood, and fragments of intestinal *débris*. Evacuation brings no relief ; the rectum may be almost empty, but the desire to expel its contents still remains, and a sensation of obstruction causes the patient to make violent and continuous efforts to clear the bowel. Tenesmus, moreover, is vesical as well as rectal ; and during acute attacks of amœbic dysentery spasm of the neck of the bladder is often one of the most urgent and distressing symptoms. As a result of excessive straining, prolapse of the rectum is a common complication of dysentery in children, and is not infrequent in adults.

Unless relieved by treatment, the condition at this period may soon become critical. Prostration increases, and the nervous system is especially liable to be affected. Lack of rest, pain, and apprehension of further suffering frequently induce melancholic depression, and acute delirium is by no means rare. In malignant cases, all the symptoms continue to increase in severity ; there is often copious hæmorrhage from the bowel ; and exhaustion sets



in, to be followed within a few hours by death from cardiac failure and collapse.

A fatal result is, however, unusual ; and even without treatment, the system is generally able to cope with a first attack of amœbic dysentery. In the majority of instances, the duration of the acute stage is only about forty-eight hours ; and evidences of improvement begin to manifest themselves within five days of the beginning of the illness. In these favourable cases pain subsides rapidly, tenesmus decreases, and fæcal matter reappears in the dejecta. Recovery, however, is rarely satisfactory or complete. Irregularity of the intestinal functions, with intermittent persistence of mucus and blood in the dejecta, indicates the continuance of the infection ; and about half of all cases of amœbic dysentery pass after the first attack into a chronic condition, in which, although during the quiescent stages dysenteric symptoms are but slightly marked, there is constant liability to relapse.

The following symptomatic characteristics may also be generally noted in amœbic dysentery :—

The TONGUE, in the acute phases, is thickly coated with white or gray fur, but after the first evacuations, the dorsum begins to clean from the edges, and as the attack progresses it quickly resumes an almost normal appearance. In the chronic stages of the disease, the tongue is generally smaller and redder than usual, although otherwise unchanged. Stomatitis, and lingual or oral ulceration, are very rare in amœbic dysentery.

At the commencement of an attack, the SKIN is dry and parched, but after one or two days it becomes unusually moist and relaxed. In most cases, a tendency to excessive perspiration persists throughout the course of the disorder ; and at times of crisis copious and exhausting sweats are induced by the incessant straining and tenesmus. In the later stages of amœbic dysentery, the com-

plexion becomes sallow, and the skin assumes the dry and muddy appearance which is indicative of intestinal toxæmia.

The PULSE and RESPIRATION are uncharacteristic, but they should be carefully watched in order to obtain timely warning of untoward complications. In the period of invasion, both are accelerated; but, with the subsidence of the fever, they resume their natural condition. During the quiescent phases of the disorder, the circulation is generally feeble, the movements of the heart abnormally slow, and the vasomotor system relaxed. A malignant type of infection is indicated by a small, rapid and jerky pulse. Almost the earliest signs of hepatic complication are increased frequency of respiration and shallow breathing, the latter being especially noticeable near the base of the right lung.

The STOMACH is but little affected in amœbic dysentery. In the earlier period of an acute attack, however, intense nausea is an almost invariable feature, and marked dyspepsia continues until the subsidence of the more urgent symptoms. During quiescence the gastric functions are unimpaired; whilst, in the chronic stages of amœbic dysentery, the excellence of the appetite is often remarkable. It is, however, uncertain and capricious; the patient becomes unnaturally hungry soon after a meal, and although the digestion appears to be unusually vigorous, it is easily deranged; unsuitable nourishment and excessive quantities of food being, perhaps, the most fertile sources of relapse. Incessant hiccough is occasionally present; but it is rarely seen except in malignant cases, and is always a symptom of grave import.

THE VASCULAR SYSTEM.—During acute attacks of amœbic dysentery there are few changes in the constitution of the blood. The red cells are unaltered in appearance and numbers, and there is little diminution in the normal proportion of hæmoglobin. The white cells are slightly increased, both actually and relatively;

but the polymorphonuclear leucocytosis, which has been described as occurring in severe infections, is certainly not invariable in the early stages. Probably, in every case in which this condition is seen, it is the result of alcoholism or of intoxication by drugs. There is no mononuclear increase, and unless there is a collateral infection of anchylostomes, or some other variety of the grosser entozoa, there is no marked eosinophilia. AMBERG<sup>1</sup>, however, found that in children suffering from amœbic infection there was an actual and a relative increase of eosinophiles.

During the later stages of amœbic dysentery, a typical form of secondary anæmia is induced by the absorption of intestinal toxins, and the alterations in the blood resemble those which are seen in chronic lead and arsenic poisoning, cirrhosis of the liver, and anchylostomiasis. Like the toxins of these disorders, the blood poison directly destroys the corpuscles in the circulation, and there is, in consequence, marked oligocythæmia and poikilocytosis. Normoblasts, megalocytes and myelocytes are frequently seen, and indicate a somewhat acute phase of the condition. The colour index is low, but the hæmoglobin, although decreased to about 60 or 70 per cent., is in greater than normal quantity in the individual erythrocytes. Blood counts, made at intervals of three months, show that the destruction of the red corpuscles and the other changes in the blood accurately correspond to the intensity of the toxæmic symptoms. When these are marked, it is not unusual to find that a cubic millimetre of blood contains no more than a million red cells; whilst in cases of moderate or ordinary severity, reduction to one half of the normal quantity is common.

In contrast to the condition of the blood in the earlier stages, a moderate degree of leucocytosis is an almost invariable accom-

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<sup>1</sup> S. Amberg: *Bull.*, Johns Hopkins Hosp., 1901.

paniment of advanced amœbic dysentery ; and, like the destruction of red corpuscles, it is relative to the severity of the toxæmic symptoms. When they are pronounced, the polymorphonuclears are especially numerous ; but, in ordinary instances, all the varieties of white corpuscles are augmented indifferently. Eosinophiles, too, are relatively and absolutely increased.

A series of twelve blood counts, in cases of moderate severity, in which the average duration of infection was three years, gave the following results :—

Red blood corpuscles	...	...	...	...	1,850,000 to 3,240,000
Leucocytes	...	...	...	...	10,500 ,, 12,000
Hæmoglobin	...	...	...	...	65 per cent.
Polymorphonuclears	...	...	...	...	60 to 65 per cent.
Large mononuclears and transition forms	...	...	...	...	10 ,, 17 ,,
Lymphocytes	...	...	...	...	20 ,, 25 ,,
Eosinophiles	...	...	...	...	5 ,, 6 ,,
Mast cells	...	...	...	...	0·4 ,,

with a few myelocytes, normoblasts, and megaloblasts in some cases.

The TEMPERATURE varies with the severity and clinical type of the disease. In mild infections, there is often little or no elevation of the normal body heat, even during the periodic exacerbations of the dysenteric symptoms. In moderate cases, with an acute onset, the temperature usually rises to 102° or 104° F. during the initial rigor ; but after diarrhœa begins a marked remission takes place, and the thermometer falls until a normal or subnormal level is reached. Persistent low temperatures are a marked clinical feature of advanced and uncomplicated amœbic dysentery. During the quiescent periods in the later stages of the disease, a morning temperature of 96·5° F., and an evening one of 97·5° F. are common ; whilst relapses, even although severe, are seldom accompanied by so much febrile disturbance as is usual in the earlier

attacks. High temperatures are occasionally recorded as a result of streptococcal infection of intestinal ulcers, and, in these cases, the fever assumes a pyæmic type, with marked exacerbations ( $104^{\circ}$  to  $105^{\circ}$  F.), in the evening. These instances are, however, rare; and, in the later stages, a rise of temperature with hectic symptoms generally foreshadows the occurrence of hepatic or some other metastatic suppuration. A sharp ascent, with or without a rigor, accompanied by acute abdominal pain and followed by symptoms of collapse, generally indicates perforation, and points to the necessity of immediate operation.

In malignant cases, the temperature rises—generally on the second or third day of the attack—to  $104^{\circ}$  or  $105^{\circ}$  F.; and the sudden elevation is concurrent with an increase in the dysenteric symptoms. In the tropics, hyperpyrexia is not uncommon; but it is almost invariably due to a collateral infection of malaria, which has assumed the pernicious type known as *crise dysentérique*. In doubtful cases, a search for the malarial parasite in the blood, as well as for *entamoeba histolytica* in the dejecta, should always be made.

The URINE is greatly diminished during exacerbations of the dysenteric symptoms, but in the periods of quiescence the secretion is generally abnormally copious. The specific gravity varies with the quantity, and the reaction is usually acid; but as a rule the kidneys are unaffected, although, in the later stages of chronic dysentery, albuminuria is not uncommon. Albumoses have also been noted in a number of cases, and their presence probably indicates the advent of hepatic suppuration. During acute attacks of amœbic dysentery, and especially when the dejecta are copious and watery, chlorides are generally absent from the urine; but, after the subsidence of the diarrhœa, they make their reappearance in increased quantities. QUINCKE and ROOS have called attention to

the fact that in amœbic desentery the urine generally contains considerable quantities of indoxyl.

The DEJECTA vary in quantity and character with the severity of the attack. In the mildest type of the disorder, there are seldom more than one or two motions daily, and these may be almost normal; in grave cases, purging is practically continuous. The voided matter is accurately indicative of the stage of the morbid process. During the period of invasion, it is copious, fluid, and fæcal; but, with the progress of the disease, it becomes scanty, and consists almost entirely of blood and mucus. When active ulceration is taking place, the dejecta contain many blood clots and shreds of tissue, and they are always extremely offensive. With the subsidence of the acute phase, they assume a more natural appearance; although even during quiescence there is usually a marked tendency to diarrhœa. In the latent stages, the dejecta are generally bulky and pultaceous, but there is no loss of colour; they contain an abundance of intestinal refuse, with, in most instances, an excess of mucus, and a little blood. Except during severe relapses, the suppression of fæcal matter is seldom marked. Throughout the whole course of the disorder, the reaction of the dejecta is alkaline.

In the latter stages of amœbic dysentery, and especially when toxæmia is a marked symptom, constipation is usual. In such cases the dejecta are scanty, desiccated, and coated with mucus; occasionally they are scybalous, and are voided with much difficulty and straining. Considerable quantities of blood, pus, and sago-like gelatinous matter are also excreted with the latter part of the motion.

When examined under the microscope, the dejecta of the acute stages of amœbic dysentery are found to contain varying quantities of food refuse, with numerous blood corpuscles, much disintegrating



intestinal epithelium, large epithelioid cells, pus, and many living *Entamæbæ histolyticæ*. In the majority of cases in the tropics, intestinal flagellates and parasitic ova are also present. Charcot-Leyden crystals are often seen.

The intestinal blood which is passed in the dejecta affords important indications of the nature of an attack, and of the general character and prognosis of amœbic dysentery. Although, under the microscope, red corpuscles may be found, practically at every period of the disease and almost in all degrees of severity, hæmorrhage is sometimes so insignificant that no red tinge is apparent in the excreta; and, in these cases, it may be inferred that the development of the lesions is slow, and that little, if any, ulceration has taken place. If the cæcum is chiefly affected, the blood is dark brown or black; when the lower segment of the colon is the principal seat of disease, it is fresh, bright red, discrete, and clotted; whilst, if it comes from above the sigmoid flexure, the blood is intimately mixed with mucus and fæcal matter, and the evacuations are dark red or reddish brown. Free bleeding indicates rapid rather than extensive ulceration; but the absence of hæmorrhage does not preclude the possibility of serious mischief, for in the gravest cases the destructive process is sometimes so swift that perforation takes place before blood appears in the motions.

Epithelium and disintegrating tissue are constantly present. During the period of invasion there is but little desquamation, as the mucosa is covered by a coating of fibrinous exudation; but when this breaks down, large numbers of disintegrating epithelial cells appear in the dejecta. In the ulcerative stages, shreds of decomposing mucous membrane and necrotic tissue from the submucosa are also abundant; and in severe cases, the dejecta, for lengthened periods, may consist almost entirely of blood and sloughs from these structures. In the advanced stages of the disease most



of the shed epithelial cells are small and mis-shapen, and give the impression that they have been prematurely overtaken by decay. Phenomenal quantities of epithelial *débris* are passed during the progress of chronic amœbic dysentery ; and, although the attacks are but slight, practically the whole of the superficial lining of the colon appears to be shed and renewed after each exacerbation of the symptoms. The epithelial cells show various kinds of degeneration. In the acute stages they are swollen and waterlogged, but at more advanced periods and when the disease is quiescent, they are usually granular and fatty. Large epithelioid cells are also often present in the dejecta. Of spherical or cuboidal form, but extremely irregular outline, these bodies are twice or three times the size of an ordinary epithelial cell ; the protoplasm is almost hyaline or finely granular ; it contains no vacuoles, and the nucleus is indistinct or invisible. The nature of these peculiar cells is uncertain ; it is generally believed that they are merely altered epithelium, but many observers deny that they are of intestinal origin, and point out that they are never seen in other affections of the alimentary tract. That statement is, however, not quite accurate, for they are occasionally present in sprue. Their importance chiefly lies in the fact that they may be mistaken for entamœbæ, but in fresh dejecta, at least, their lack of movement readily distinguishes them from living organisms.

Pus is often present during the later stages of amœbic dysentery. When scanty and distributed through the motion it suggests ulceration—probably superficial, and always of some standing ; when in considerable quantity it indicates submucous suppuration, or destructive and extensive ulceration. Pus cells from deep abscesses are generally identical in appearance with polymorphonuclear leucocytes.

The presence of *E. histolytica* is the distinctive feature in the

dejecta of amœbic dysentery. The organisms may be found at all periods of the disease. Their morphology and biological relations have been already described.

The PHYSICAL SIGNS OF AMŒBIC DYSENTERY are uncharacteristic. During acute attacks there is generally great tenderness over the whole length of the colon, and pain on pressure is especially marked in the sigmoid region. The abdomen is at first flatulent and distended ; but, with the onset of diarrhœa, it becomes lax and retracted. In most cases the liver is enlarged ; sometimes in the earliest stages it is notably increased in size, and there are other evidences of hepatitis. At a more advanced period the liver generally becomes smaller, and thickening of the colon is almost invariably perceptible. In chronic amœbic dysentery the abdominal muscles are unusually flaccid and attenuated, and engorgement of the intestinal walls can often be readily made out by simple palpation. There is a distinct feeling of deep resistance which accurately corresponds with the position of the bowel, and, in many instances, bosses and knobs of infiltration can be felt on the surface of the colon. The results obtained by percussion are seldom of much value.

MILD INFECTIONS AND LATENT TYPES OF AMŒBIC DYSENTERY.—In about 30 per cent. of all cases of amœbic dysentery there is no acute stage of invasion, and the onset of the illness is indefinite and insidious. So slight is the initial disturbance of health that, in many instances, the patient scarcely realizes that he is unwell ; and after death it is by no means unusual to find evidences of long continued destruction of the mucosa and sub-mucosa, although during life there were few indications of active disease. Amœbic infection frequently persists for many months or years without marked symptoms of dysentery ; and occasional abdominal discomfort, a tendency to irregularity of the bowels, and slight seizures of dysenteric diarrhœa alternating with long

intervals of unbroken health may be the only clinical signs of the formation of extensive intestinal lesions.

When carefully investigated, however, the mildest cases seldom fail to supply definite evidence of the true nature of the infection. Lassitude and periodic gastric derangements are naturally attributed to dyspepsia or inaction of the liver, and little notice is taken of what appears to be but passing indisposition; but if, during one of these attacks an examination is made, it will generally be found that considerable quantities of mucus are being voided with the dejecta, that the fæces contain large numbers of *entamœbæ*, and that there is perceptible tenderness and thickening of the colon.

These latent cases are important in that a small proportion of them unexpectedly develop a sudden increase of virulence, and an unanticipated tendency to malignancy. The occurrence of an acute relapse, after complete cessation of symptoms for two or three years, is by no means infrequent; and in such instances the type of infection is generally greatly intensified. A considerable number of cases have been reported in which amœbic dysentery, contracted in the tropics, caused little inconvenience there, and was apparently completely cured by return home; but, after two or three years in a temperate climate, the disease recurred in a severe and often fatal form.

Still another type of amœbic infection is characterised by unusual latency of symptoms, although a dangerous and extremely insidious form of ulceration accompanies its progress. Here, the lesions are more limited, the usual morbid change being chronic catarrh of the colon, with a single deep ulcer situated, in most instances, in the upper sigmoid region. This clinical variety of the disorder is generally associated with outdoor life, and is exceptionally prevalent among the numerous Europeans who are engaged as planters, engineers, mining prospectors, surveyors, &c., in agri-

cultural and pioneering work in the Eastern tropics. Repeated exposure to chills and wet can scarcely be regarded as a sufficient explanation for the frequency of this type of amœbic dysentery, and it is difficult to account for the peculiar distribution, but it is undoubtedly the case that when contracted in country districts the disease exhibits a special tendency to become chronic and latent.

The symptoms are intermittent diarrhœa, persisting irregularly for months or years, chronic gastric derangement, and occasional attacks of acute pain at a particular point in the lower abdomen. The dejecta are loose and watery, frequently pale coloured, and scanty; and they contain an excess of mucus, in which entamœbæ are invariably present. At considerable intervals there may be hæmorrhage from the bowel, bleeding being occasionally very copious. Unless the condition is aggravated by unfavourable influences, the patient is seldom confined to bed, and the symptoms cause little concern.

In the great majority of cases, amœbic dysentery, when it assumes this form, is easily treated, and complete although long delayed cure is ultimately established; but in some instances, and often when recovery seems to be assured, perforation of the bowel suddenly takes place. It is for this reason that the mildest cases of amœbic dysentery require careful supervision, and whenever there is evidence of localized ulceration, absolute rest and strict dietetic precautions should be enjoined.

**CHRONIC AMŒBIC DYSENTERY.**—Although most latent cases are, properly speaking, chronic, it is usual to describe as chronic amœbic dysentery those instances of amœbic infection in which the passage of mucus and blood is the most prominent characteristic. The condition is generally one of moderate gravity; the bowels, in the absence of effective treatment, continue to be irregular, and constipation alternates with diarrhœa. At such times there are four,

five, or more motions daily; some of them—usually those passed in the morning—contain considerable quantities of slime and blood, but the others may be almost normal. The patient complains of intermittent pain in the sigmoid region; as a rule, the calls to stool are urgent, and there is often partial paralysis of the sphincter ani. During the attacks gastric symptoms are prominent and headache is especially frequent and severe. The tongue is generally small, dry, and coated with brownish fur; and much distress is caused by persistent dyspepsia, flatulence, and the involuntary passage of small quantities of intestinal matter.

In many cases indications of constitutional disturbance make their appearance and, after some months, toxæmia of the definite type which is associated with intestinal auto-infection becomes fully established. The onset of toxæmia is attended by failure of nutrition, progressive anæmia, and emaciation due to absorption of subcutaneous fat. The skin is dry, inelastic, and flabby; the muscles are lax and atrophied. Loss of weight is always considerable, and, occasionally, it is very great. The facies is characteristic. Owing to the loss of orbital fat, the eyes appear unnaturally large and prominent, but they are dull and tired looking; the expression is listless and careworn; the complexion sallow, or even saffron coloured, with muddy patches of pigmentation on the cheeks and under the angle of the jaw. There is often marked inequality of the pupils.

The blood changes have already been noted. The reflexes, both superficial and deep, are sluggish, and their excitability is much diminished; the pulse is generally slow, and always of low tension; the urine is scanty, high-coloured, and loaded with urates.

In extreme and neglected cases, these manifestations are gradually progressive, and a condition of chronic marasmus supervenes. The deterioration in general health is seldom accompanied by a marked

increase of the dysenteric symptoms, and death is almost always due to the continued absorption of intestinal toxins. In the advanced stages of toxæmia, depression of the vital functions is extreme ; the patient lapses into an apathetic state, and is indifferent to his comfort and surroundings ; bedsores form readily, and the lips become dry, cracked, and covered with sordes. Ultimately, the heart begins to fail ; the pulsations are accelerated, irregular, and lacking in force ; albumin appears in the urine, and the lower extremities are swollen and œdematous. Marked symptoms of meteorism usually precede a fatal issue ; the abdomen is inflated and resonant, the colon tympanitic ; small quantities of loose and foetid dejecta are passed involuntarily, and often almost continuously ; prostration gradually increases, and, after a short period of unconsciousness, death results from paralysis of the cardiac muscle.

Happily, however, most cases of chronic amœbic dysentery tend to a more favourable termination. Even without active treatment, although an advanced stage of the disease has been reached, complete recovery is by no means unusual ; whilst, in the absence of complications, and if the disorder is taken in hand before toxæmia sets in, the percentage of cures is a high one. In favourable instances, the dysenteric symptoms gradually become less accentuated with each recurrence of the disorder ; nutrition slowly improves ; and, although liable to gastric and intestinal derangements, the patient frequently lives to enjoy good health for many years.



## CHAPTER XI.

## DIAGNOSIS.

THE absolute diagnosis of amœbic dysentery rests on the discovery of entamœbæ in the dejecta; and when these are found, the disease is clearly distinguished from all other intestinal derangements. Apart from the actual demonstration of the parasite, however, the clinical features of various other affections sometimes closely resemble the symptoms of amœbic dysentery; and for purposes of prognosis and treatment the timely differentiation of these conditions is of material importance.

The disorders which are most liable to be confused with the acute manifestations of amœbic infection are bacillary dysentery, the dysenteric form of pernicious malaria, hæmorrhagic typhoid, intussusception, and other mechanical obstructions of the bowel. The advanced stages are often closely simulated by chronic bacillary dysentery, by intestinal catarrhal inflammation, by schistosome infection, by tubercular ulceration of the intestine, and by malignant disease of the lower bowel.

*Bacillary Dysentery.*—Although the tendency of bacillary dysentery is to assume a more acute form, its distinction from the amœbic variety of the disease, both in the earlier and later stages, depends almost entirely on the result of microscopical investigation. Relapse and recurrence, if somewhat less frequent in the former, are common to both infections; and although the severity of the symptoms, the character of the hæmorrhage, and the appearance of the dejecta



are suggestive, they seldom afford any definite information as to the true nature of the illness.

The following histological distinctions are important:—

(1) In bacillary dysentery, a fragment of matter taken from the dejecta generally contains: (a) Long hyaline fibres of mucus. (b) Numerous red blood corpuscles. (c) Much desquamated epithelium. (The cells are frequently waterlogged, and are often mistaken for entamœbæ.) (d) Large numbers of leucocytes, with a considerable relative predominance of mononuclears. Phagocytosis is generally active. (e) Bacteria in great abundance and variety.

(2) In amœbic dysentery a similar preparation usually shows: (a) A comparative scarcity of leucocytes, with marked relative increase of polynuclears and eosinophiles. (b) Fewer free blood corpuscles and bacteria. (c) Living or encysted entamœbæ. The organisms are most numerous round the edges of the flecks of mucus, and in the liquid part of the evacuation. Many of them contain blood corpuscles, bacteria, and other matter which has been englobed by their protoplasm.

Further assistance in diagnosis may be rendered by the results of bacteriological and transmission experiments. In bacillary dysentery, when cultures of the dejecta are made on DRIGALSKI'S medium, the developing colonies of *Bacillus coli* are red, those of *B. dysentericæ*, blue. Moreover, in all but the mildest cases, the blood-serum develops agglutinative properties about the eighth day of the disease; and tests made with the SHIGA bacillus, in not less than 1 to 30 dilution, and with the FLEXNER in 1 to 80, give positive results. In amœbic dysentery, on the other hand, DRIGALSKI cultures and agglutination experiments are negative; but the disease and the growth of organisms can be reproduced in a kitten by the rectal injection of a minute quantity of evacuation.

*Pernicious Malaria.*—The occurrence of dysentery as an *accès pernicleux* of malaria is denied by many authorities ; but there can be no question that in regions where dysentery is endemic a dysenteric crisis frequently develops during a seizure of malignant malaria. The identification of the actual condition is important. If the symptoms originate in malarial infection, life may be saved by the timely administration of quinine. On the other hand, if the dysentery alone is treated, the case will, almost certainly, prove fatal.

Amœbic dysentery and malaria may, however, be combined in the same patient ; and the dysenteric symptoms, although not actually a result, are always aggravated by the co-existence of malarial infection. Some information as to the influence of the respective factors may be afforded by the use of the thermometer, but temperatures are not always high or intermittent in malaria and low in dysentery. The blood is the only reliable diagnostic index, and in every case of dysentery when malarial infection is possible, films should be prepared and carefully searched for the presence of the parasite.

In tropical practice, dysentery is often seen as a terminal symptom of many widely different pathological conditions ; and in tuberculosis, diabetes, Bright's disease, and the severe anæmias, it is by far the commonest ultimate cause of death. It occurs, for the most part, in ill-nourished subjects, and is a frequent and fatal complication of the cachectic marasmus which originates in chronic and repeated malarial infection. In these cases, however, entamœbæ can rarely be detected in the dejecta, and the symptoms and pathological appearances seldom suggest amœbic disease. Probably in terminal dysenteries the infection is always bacterial.

*Hæmorrhagic Typhoid.*—In the tropics, also, the clinical manifestations of enteric fever are generally atypical, and considerable

quantities of intestinal mucus are passed at intervals throughout the whole course of the disease. During the early stages, the excretion of mucus is sometimes so marked as to suggest a combination of dysentery and typhoid; and it is especially prominent in those cases which are afterwards complicated by severe bleeding. In these patients, too, the temperature, eruption, and other symptoms are frequently uncharacteristic, and there is, in fact, often great difficulty in arriving at a conclusion as to the actual condition.

It should be remembered, however, that in many of these instances typhoid infection is not assured. Sometimes, at any rate, bleeding depends on a hæmorrhagic diathesis, and numerous cases have been reported<sup>1</sup> in which the initial symptoms were those of dysentery; but the hæmorrhage from the bowel proved to be a precedent of general purpura and severe bleeding from other mucous membranes.

Still more uncertain is the true pathology of a form of ulcerative colitis first accurately described by Professor OSLER. The clinical features of this condition—which is not uncommon in the tropics—resemble those of severe typhoid. The symptoms are high fever, prostration, pain, frequent hæmorrhagic evacuations, and, in many cases, violent delirium. Entamœbæ have been observed, but are infrequent. As diagnostic points, OSLER instances a normally sized spleen, and the absence of rose spots. Widal's reaction may also be of some assistance; but in the Eastern tropics these signs are inconstant and unreliable.

Cases occasionally occur which indicate the possibility of combined infection. In a recent instance the patient, who had been ill for over four weeks, was passing large quantities of mucus and

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<sup>1</sup> See Blair, *Lancet*, January 14, 1905; Strong, and others.

blood. No entamœbæ could be found, although at the beginning of the illness they were reported to be present in considerable numbers. Widal's reaction was negative, but there was marked lymphocytosis. Although the temperature was sometimes high, it was irregular and uncharacteristic; and other indications being indefinite, the disorder was diagnosed as amœbic dysentery. At the end of the fifth week severe hæmorrhage occurred; and death, which was due to exhaustion, took place on the fiftieth day. At the autopsy, Peyer's patches were found to be engorged and extensively ulcerated, although the colon and other viscera were intact, and no entamœbæ of any kind could be discovered. Large numbers of *Bacillus typhosus* were found in spleen cultures.

*Intussusception*, impaction of scybalous matter, and other mechanical obstructions occasionally give rise to symptoms of acute dysentery; and these conditions, together with various forms of alimentary intoxication, must be remembered as possible sources of error in diagnosis. In hot climates, the consumption of shell-fish, unripe fruit, or decomposing food is prone, not only to induce a temporary dysenteric derangement, but to transmute a latent amœbic infection into an acute and, possibly, malignant attack of dysentery. Examination of the abdomen and dejecta generally reveals the nature of the illness, and there is seldom any difficulty in recognizing these accidents, or in determining their influence on the symptoms.

*Chronic Catarrh of Non-parasitic Origin.*—In its clinical aspects, a form of mucous colitis which is common in warm countries occasionally resembles the less active phases of amœbic dysentery very closely. Pathologically, the disorders are widely differentiated; but the symptoms are often so much modified that the conditions are liable to be confused.

In these cases, intestinal irregularity, with an excessive secretion

of mucus, is the most prominent feature. There may be diarrhœa, the dejecta being often intermixed with large quantities of glairy discharge; or there may be periods of excessive constipation, when the evacuations are scanty and scybalous. The intestinal concretions are, for the most part, embedded in dense coils of gelatinous matter which is generally thickly streaked with blood. In some instances, masses of sanguineous mucus are passed at intervals during a long term of years; and although at these times there are acute exacerbations of pain, there are no other indications of intestinal disease. *Entamœba* and *Bacillus dysentericæ* can never be found.

Some light may be thrown on the true nature of the disorder by the fact that, in catarrhal colitis, the dejecta are seldom offensive, that the mucus in most cases is unusually hyaline, hard, and fibrous, and that pus is always absent; but unless specific organisms can be demonstrated, diagnosis between mucous colitis and chronic dysentery is often impossible.

*Helminthiasis*.—Some forms of trematode infection simulate the symptoms of dysentery so closely that they are often described as varieties of that disease. Such are the parasitic disorders known as opisthorchiasis—infection by intestinal flukes of the genus *Opisthorchis* (principally *O. sinensis*); and bilharziosis—invasion of the circulation by two species of blood-fluke (*Schistosomum hæmatobium* and *Schistosomum japonicum*).

*Opisthorchis* and *Schistosomum japonicum* are comparatively unimportant parasites; they are rarely harboured by Europeans, and are seldom encountered except in Far Eastern Asia. Bilharziosis, on the other hand, is widely distributed throughout the tropical and subtropical regions of Africa, Asia, and America; it is especially prevalent in Egypt where it frequently attacks both Europeans and natives; and its endemic area appears to be rapidly increasing. In all these infections, the passage of blood and mucus, with recurrent



seizures of pain and dysenteric diarrhœa, are prominent features ; and, in most cases, the disease ultimately proves fatal, its duration varying from a few months to many years.

Similar manifestations occasionally follow the attachment of ankylostomes and other nematode entozoa to the intestinal walls, but dysenteric symptoms seldom develop unless these worms are present in exceptional numbers. In cases of marked helminthiasis, there should be no difficulty in recognizing the condition and in determining the species of parasite. When the dejecta are dysenteric in character, the excretion of distinctive ova is almost continuous and invariable, and the eggs are readily identified by the microscope.

*Intestinal tuberculosis* is common in many districts where amœbiasis is endemic ; and, in the Eastern tropics at all events, tubercular ulceration is frequently mistaken for chronic dysentery. The cæcum, with the investing peritoneum, is especially liable to attack, but the morbid process rarely extends below the upper third of the colon. ROGERS<sup>2</sup> has tabulated the sites of disease in 509 fatal instances of tuberculosis in Bengal, and has shown that, in about 8 per cent. of all cases, the lesions are intestinal or peritoneal. The relative incidence of tuberculosis of the alimentary tract is as sixty-five in India to twenty-three in England ; whilst, of 133 cases treated in the General Hospital, Calcutta, the small intestine was affected in all, and the large in 118. In Java, the proportional frequency is, practically, the same ; whilst KITASATO has recorded the significant observation that in Japan, where cow's milk is never used for feeding infants, intestinal tuberculosis is at least as prevalent as in Europe.

The symptoms of tubercular infiltration of the great intestine are intermittent pain with occasional attacks of severe colic,

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<sup>2</sup> Professor L. Rogers, *Indian Medical Gazette*, February 2, 1909 ; see also report of discussion at the Royal Asiatic Society (Bengal), February, 1909.



irregular fever, and looseness of the bowels. As the mucosa ulcerates, the diarrhoea becomes dysenteric in character, there is usually great tenderness in and around the right iliac fossa, and recurrence alternates at uncertain intervals with lengthened periods of relief. Perforation and pericæcal abscess are frequent complications; and at this stage the general symptoms of tubercular ulceration often accurately resemble those of amœbic disease.

An important diagnostic feature is the fact that in dysentery the ulcers usually extend throughout the whole length of the colon, and that there is marked tenderness over the sigmoid flexure rather than in the cæcal region. Diagnosis on clinical grounds alone is, however, always very doubtful, and differentiation between the two conditions may be practically impossible.

*Malignant disease of the sigmoid and rectum* is prevalent in most warm climates. It is seen in all races, but Europeans who have had a lengthened residence in the tropics, and who have suffered from dysentery or proctitis, are especially liable to be affected. At an advanced period the true nature of the disease can scarcely be mistaken; but the first indication of carcinoma of the lower bowel is, not infrequently, a succession of subacute dysenteric attacks.

In such cases the initial symptoms are generally those of irritative diarrhoea. The evacuations are small but frequent; and, after two or three days, they consist for the most part of mucus, blood, and pus. Fæcal matter is scanty, and often altogether absent from several successive motions. Tenesmus is usually a distressing feature. The symptoms gradually subside within a week, but generally recur several times without definite evidence of obstruction.

In elderly patients the possibility of malignant disease should always be borne in mind and before making a diagnosis the rectum should be thoroughly explored.



PART IV.—PATHOLOGICAL.



## CHAPTER XII.

### MORBID ANATOMY.

THE pathological changes which are found in amœbic dysentery vary to some extent with the intensity of the morbid process and the duration of the illness, but, in the great majority of instances, they are characteristic of the infection and are readily distinguished from those of all other intestinal disorders. Uniformity of pathological type is especially marked when the course of the disease has been prolonged, and evidences of amœbic invasion are always most distinctive and conclusive when relapses have been numerous and frequent. On the other hand, in acute cases, when inflammation is extensive, and absorption of toxins is so rapid that death results from shock before the stage of ulceration is reached, the gross lesions are often uncharacteristic; and, when malignancy is extreme, even after careful microscopic examination of the tissues, there may be some doubt as to the actual nature of the infection.

### MALIGNANT AMŒBIC DYSENTERY.

The morbid changes in malignant cases are indicative of intense inflammatory reaction throughout the whole length of the colon. They differ from the lesions of the commoner clinical form of amœbic dysentery not only in degree, but also in that the superficial structures are more severely affected. In rapidly fatal instances, both of bacillary and amœbic dysentery, the mucous

membrane is invariably hyperæmic and inflamed, but the changes in the submucosa are much less conspicuous in the acute than in the chronic form of the latter disorder.

So far, indeed, as can be seen by the naked eye, when the disease assumes a malignant type the gross lesions of all varieties of dysentery present a remarkable similarity. On opening the colon, the mucosa is found to be intensely engorged and swollen; it is dark blue or purple in colour, with extensive arborizations of congested vessels, and numerous extravasations are scattered over the surface. At this stage there is seldom any ulceration or evidence of deep suppuration; but points of superficial necrosis, many of them already beginning to break down, are abundant. There is always an excess of mucous secretion; and, here and there, patches of exudate become closely incorporated with the disintegrating mucosa, and unite with it to form diphtheritic membranes.

When malignancy is less pronounced, it is seen that the resemblance between the post-mortem appearances of acute amœbic and bacillary dysentery is only superficial; and examination of the tissues under a low power generally reveals the essential difference of the morbid process. In bacillary dysentery—in which the fulminating type is common—the disease remains centred in the mucosa, and inflammation extends from the surface downwards. In amœbic infections malignancy is infrequent, and the submucosa, in cases which are not immediately fatal, is invariably affected, extension taking place from below upwards.

Vertical sections also show that in bacillary dysentery the epithelial structures are specially selected for attack, whilst, during the earlier stages at least, the submucosa is practically unaffected. The inflammation of amœbic dysentery, on the other hand, begins in the submucosa; and, after reaching the mucous membrane, is most accentuated in its lower segment. Moreover, with a higher mag-

nification, the centres of infiltration and incipient necrosis in both structures may be shown to originate in an invasion of *Entamæba histolytica*; and, in most cases, the organisms themselves may be readily demonstrated.

### RECURRENT AMŒBIC DYSENTERY.

(I) *Stage of Invasion*.—Opportunities for investigating the early lesions of ordinary cases of amœbic dysentery are infrequent; and it is but rarely that the morbid appearances can be studied in the human intestine during the stage at which they are most instructive. The results of a series of autopsies on prisoners in Manila jail, who succumbed to an epidemic form of pneumonia, and recent observations by JÜRGENS and other writers have, however, shown that the following changes are perhaps invariable :—

(i.) In the mildest cases—as in all other types of amœbic dysentery—the submucosa is the structure principally affected.

(ii.) Unless the onset of the disease is of an exceptionally malignant character, the lesions of the mucous membrane are clearly secondary to those of the submucosa.

(iii.) The morbid processes of acquired amœbic dysentery in man closely correspond to those which result from the experimental infection of cats.

In the early stages of amœbic dysentery, when the initial attack is of moderate severity, the gross abdominal lesions are unimportant. The peritoneum is injected, and usually contains an excess of serum in its cavity; but there is seldom any marked evidence of general or localized inflammation, and in many cases the other viscera appear to be almost normal.

The great intestine is, however, always altered in appearance; the colour is brighter than usual, the serous covering being exceptionally smooth and glistening, and numerous small patches of



congestion and vascular stasis may be seen through the peritoneum. On opening the colon, the mucosa is found to be little, if at all, inflamed; but there are generally some points of hyperæmia and ecchymosis, with an excess of mucous secretion on the surface. There is a loss of flexibility and a definite increase in the opacity, thickness and resistance of the walls, with a boggy feeling on pressure; and, if the bowel is closely examined, it will be seen that these changes are principally due to alterations in the submucosa.



FIG. 20.—*Entamoeba histolytica* in tissue. Section of submucosa of colon, fixed in corrosive sublimate and alcohol, and stained with nigrosin. Three entamoebæ may be seen following each other in a tunnel which the leader is excavating. *E*, Entamoebæ; *G*, glandular tissue (disintegrating); *L*, small cell infiltration.  $\times 350$ .

Most writers are agreed that the first incident in the development of human amœbic dysentery is the assembly of large numbers of entamoebæ in the follicles of Lieberkühn, and that, although catarrh of the mucosa is more accentuated in man, the subsequent processes

are practically the same as those which are seen in cats. The organisms penetrate the walls of the crypts by thrusting their sharp pseudopodia between the epithelial cells, afterwards traversing the basement membrane, and burrowing into the submucosa. Sections show that for some distance they mostly follow the same tracks; and chains of entamœbæ may often be seen lying in sinuses which, apparently, have been tunnelled out by the leader. Ultimately they diverge and, pushing into the tissues, come to rest, singly or in groups of two or three.

Recent observations by DOPTER<sup>1</sup> indicate that there may be other routes of attack. He has shown that the development of entamœbæ in the lumen of the human colon is followed by hyperæmia of the mucous membrane, and that a copious secretion of viscid mucus takes place from the glands. He believes that the organisms are, in consequence, unable to enter the crypts of Lieberkühn, and that they penetrate the mucosa direct from the intestine. They have thus to traverse the whole thickness of the interglandular tissue before they reach the submucosa, and their passage is attended by considerable disturbance and cellular infiltration. DOPTER further considers that, in man, the epithelium of the crypts is never destroyed primarily, but that it is attacked from behind by organisms which have effected a direct entrance. His sections, however, are somewhat inconclusive; and there is abundant evidence that this route of invasion is by no means the most common.

(2) *Stage of Pre-ulceration*.—In the mildest cases, temporary or permanent cessation of the morbid process occurs almost immediately after invasion. Fresh immigrations of organisms from the alimentary canal are arrested, whilst those already embedded in the tissues die and become absorbed without leaving any trace of

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<sup>1</sup>Ch. Dopter, "Anatomie pathologique de la dysenterie amibienne," *Archives de Médecine expérimentale*. July, 1907.

their presence. When conditions more favourable to their development are encountered, inflammation extends rapidly. The entamœbæ receive continuous additions to their numbers from the lumen of the intestine; those already in the submucosa multiply by schizogony, and the islands of congestion coalesce to form large patches of infiltrated tissue.

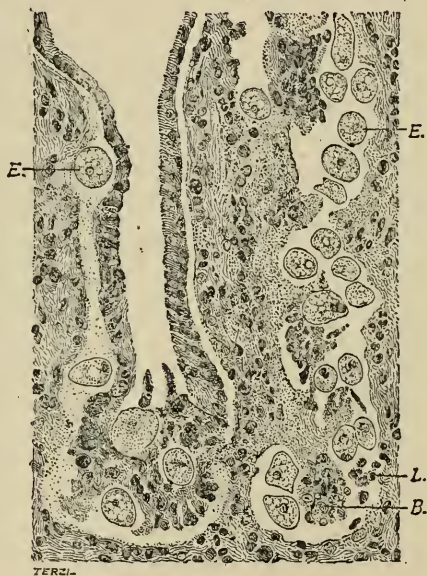


FIG. 21.—*Entamoeba histolytica* in mucosa of colon. Invasion of the crypts of Lieberkühn from the interglandular tissue, and subsequent destruction of epithelium by the organisms. *E*, Entamœbæ; *L*, small-cell infiltration; *B*, blood corpuscles and debris.  $\times 300$ . (After Dopfer.)

Evidences of further reaction are soon apparent. The walls of the intestine become congested and thickened; the mucosa is catarrhal and partially concealed by viscid mucus: and, in severe

cases, patches of false membrane cover the surface. The submucosa, however, continues to be the principal seat of inflammation; and it is generally extensively affected. Not only is it actively inflamed and infiltrated, but the connective tissue fibres proliferate, and minute buttons of adenoid tissue push up from below and appear as clusters of wart-like buds on the surface of the mucous membrane. At a later stage, the central areas of these protuberances suppurate; and none of the morbid changes of amœbic dysentery are more distinctive of the disease than the exudation of pus from minute orifices on the apices of mammillated growths on the mucosa. These suppurating adenoids are generally plentiful at the lower end of the colon; and, in cases in which the use of the sigmoidoscope is justifiable, they may sometimes be demonstrated in the sigmoid flexure.

At this stage also, numerous erosions and points of necrosis appear on the mucosa. At first superficial and discrete, they gradually coalesce, extend, and deepen, until they include considerable areas of the surface. These points usually constitute the centres of ash-coloured patches, which are covered by ecchymoses and other appearances indicative of strangulation, and which ultimately break down to form the typical ulcers of amœbic dysentery. Between them the mucous membrane is normal, except for the arborizations of congested vessels, which at this stage are thickly distributed over the surface.

Deeper in the mucosa, evidences of strangulation are still more plentiful. If a section is made into the submucosa at the base of one of the patches, the results of pressure and infiltration are everywhere apparent. The capillary circulation is almost completely arrested, and owing to stasis in the smaller arterioles and subsequent extravasation of blood and serum, the tissues are sodden and œdematous. Not infrequently, points of suppuration may be seen,

which, at a later stage, unite to form small abscesses. These collections of pus have seldom any definite limits or abscess walls ; they communicate freely with each other by tortuous sinuses, and the contents of the cavities soak through the tissues in every direction, ultimately finding an exit on the surface of the mucosa.

Under medium powers of the microscope, the further progress of amœbic infection can be readily followed at this stage. Arrived in the interglandular tissue, the organisms push down to the submucosa, their tracks being easily recognizable by the detritus of necrosed cells and the infiltration which mark the lines of their passage. In sections, entamœbæ seem to be surrounded by clear spaces ; but in most cases these apparent cavities are the result of shrinkage which takes place during hardening of the tissue. It is, however, undoubtedly true that the mere contact of *Entamœba histolytica* with a connective tissue cell may be sufficient to cause the death of the latter ; and that, in these circumstances, hyaline degeneration is the common form of necrosis.

Two distinct varieties of tissue destruction result from the invasion of entamœbæ. They are coagulation necrosis and suppuration. The first commences in a copious effusion of sero-fibrinous fluid in the submucosa, during which enormous numbers of wandering corpuscles collect in the spaces of the connective tissue and surround the minute blood-vessels and lymph-channels into which the entamœbæ have penetrated. The circulation is gradually arrested by the increasing density of the infiltration ; and, at the points where stasis is complete, blocks of connective tissue cells undergo hyaline degeneration. Their outlines fade and become indistinct, and the protoplasm loses its granular appearance. Ultimately, the effusion is, to a large extent, absorbed, and the fibrin coagulates to form numerous interlacing bands of contractile tissue, in the meshes of which the infiltrated cells are further



compressed and disorganized. Except for entamœbæ, and remnants of the solitary and epithelial glands, the necrosed tissues and vascular walls are structureless, homogeneous, and impervious to stains.



FIG. 22.—Coagulation necrosis and commencing ulceration. Section through the mucosa of the colon in the secondary stage of amœbic dysentery. The mucosa in the centre of the figure has been disorganized, and all glandular structure has been obliterated by the coagulation; but, at the edges of the patch, the remains of Lieberkühn's crypts may be seen in various stages of degeneration. A few single entamœbæ are scattered through the necrosed tissue.  $\times 120$ . (After Dopter.)

There are few polymorphonuclear cells in the infiltration, their infrequency at this stage of amœbic infection being very remarkable. The predominating cellular elements are lymphocytes; but in many cases there are also large numbers of eosinophiles, a combination which, as has been pointed out by MUIR<sup>2</sup> is indicative of chronic and persistent inflammation. Coagulation necrosis is induced partly by the toxic influence of the entamœbæ, but chiefly by

<sup>2</sup> *Brit. Med. Jour.*, 1904, vol. ii., p. 585.



strangulation of the tissues in the submucosa. The process, once established, is a rapid one. Where pressure is greatest, the overlying mucous membrane quickly becomes involved, and the follicles and epithelial cells are almost immediately disorganized by the arrest of the circulation.

In the second variety of entamœbic tissue destruction, suppuration is the predominant feature. Probably in every instance it is the result of microbial infection; for, in coagulation necrosis, the tissues may be sterile. Small-cell infiltration is, primarily, protective, and seldom tends to suppuration; but if pyogenic bacteria are introduced by the entamœbæ, the formation of pus almost invariably follows.

The lymph sinuses, the vascular sheaths, the vessels around the solitary glands, the smaller veins, and the connective tissue lacunæ where entamœbæ have lodged are chiefly affected; and, in chronic cases, these channels are almost invariably distended by sanious and offensive pus. Free communication is opened up by the lymphatics, and by the burrows of the organisms; and, although the overlying mucous membrane may be intact, large patches of the submucosa break down into networks of suppurating sinuses. Sooner or later, however, lateral extension is blocked by increasing pressure or by thrombi in the vessels; and, at the point of occlusion, a pocket of pus bulges up into the muscularis mucosæ and finally burrows a passage to the surface. Not infrequently, the tissues are so devitalized that the mucosa over the abscess sloughs away *en masse*, and the cavity is at once converted into an amœbic ulcer. Only in rare instances does encystment or caseation take place at this stage.

Sections show that, during this process, the vascular and lymphatic systems of the submucosa are always profoundly affected. The vessels become tortuous, dilated, and thickened; in most cases,

the endothelium is shed, and dense thrombi, formed of corpuscles, coagulated lymph, and entamœbæ, block the lumen. At this stage of the morbid process, however, entamœbæ are very difficult to identify, and unless the preparation is properly stained they may be easily confused with endothelial cells or other morbid products. The closed follicles are generally inflamed and infiltrated, but show no distinctive alteration. Only in exceptional instances do they contain entamœbæ.

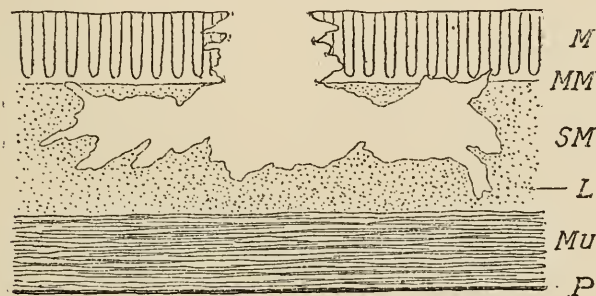


FIG. 23.—Schematic representation of an amœbic ulcer. *M*, Mucosa; *MM*, muscularis mucosæ; *SM*, submucosa; *L*, infiltration by lymphocytes; *Mu*, muscular coats; *P*, peritoneum.

(3) *Stage of Ulceration*.—Most distinctive of all the characteristics of amœbic dysentery is the type of ulceration seen in the advanced stages of the disease. Originating in sloughs of the intestinal wall which have been devitalized by coagulation necrosis or suppuration, the ulcers always show, in comparison with their superficial area, an excessive destruction of deep tissue, the loss being greatest in the submucosa. Not only is that structure the favourite site of first attack, but it is more readily impaired by the entrance of the organisms than are the other coats of the intestine. The conse-

quence of amœbic invasion, therefore, is that the tissue breaks down easily, and "undermining"—the classical distinction of amœbic ulceration—takes place. Large cavities form beneath the edges as a result of disproportionate excavation in the submucosa, and the overhanging margins, ragged and swollen, float free in the lumen of the intestine.

If a section is made through the centre of an eroded patch, it will be seen that the necrosed portion of the surface is continuous with a more extensive area of destruction in the submucosa; and, when the slough separates, the opening is, in consequence, much smaller than the base of the ulcer. Around the aperture, the intestine is generally much thickened by repeated infiltration, and, as the edges break down, a corresponding increase in the size of the cavity is maintained by further loss of deep tissue. At its formation, an amœbic ulcer may, in fact, generally be compared to a Florence flask, with the fundus resting on the circular muscle, and the neck opening on the surface of the mucosa.

Although this infundibular shape is almost invariable in the later stages of amœbic dysentery, ulcers of a somewhat different conformation are occasionally seen in the earlier periods of the disease. Originally described by HARRIS, they are known as the "ulcers of Harris," and are usually situated on the ridges of the folds of the mucosa. They are generally superficial, rarely reaching to the muscular coat, and never penetrating it. The edges are clean cut and abrupt, and the appearance is suggestive of a circular patch of mucous membrane having been sharply punched out. There is little destruction of tissue, and although MUSGRAVE and WOOLLEY regard them as being intermediate stages between the petechial erosions and the undermined cavities, there is some doubt as to their nature, and especially as to their connection with amœbic infection.

*Amæbic Ulcers.*—Typical amœbic ulcers vary in size ; sometimes they are small, no bigger than a millet-seed ; more often they are the size of a pea ; whilst still more frequently, when the bowel is much infiltrated and thickened, they are as large as a filbert. Individual primary ulcers seldom exceed those dimensions, and the huge patches seen in the later stages are always the result of coalescence. In such cases, large areas of submucosa are destroyed by the deep junction of ulcers, the orifices of which are

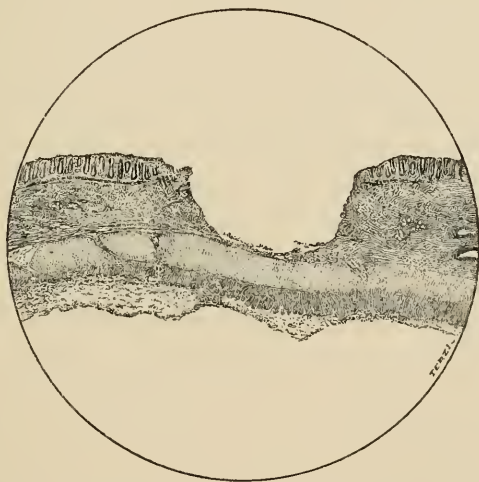


FIG. 24.—Section of intestine from a case of amœbic dysentery, showing a typical “ulcer of Harris.”  $\times 45$ .

only minute openings in the mucous membrane—the *ulcères en bouton de chemise* of French writers—and, although a probe may be passed to its full length in almost any direction, the mucosa itself often appears to have suffered comparatively little damage.

For some time after their formation, the bases and walls of

amœbic ulcers are covered with ragged shreds of decomposing sloughs which secrete an offensive discharge of ichorous pus, serum and blood; but, by degrees, the necrotic tissue is shed, and the cavity of the ulcer assumes a more healthy appearance. If a scraping of slough or a minute drop of discharge be examined at this stage, large numbers of entamœbæ may generally be seen actively moving about among the pus corpuscles. Organisms are especially numerous in the tissue immediately surrounding the ulcer, and the so-called pyogenic membrane often appears to consist almost entirely of entamœbæ. When ulceration is a result of coagulation necrosis, the adjacent tissues contain enormous numbers of disorganized lymphocytes and connective tissue corpuscles enclosed in a stroma of lymph fibrils. Round the margins of the patch, nests of entamœbæ may generally be found in abundance.

The toxins secreted by entamœbæ seem to be as fatal to microbial life as to connective tissue cells, and bacteria are seldom seen in the tissues during the pre-ulceration stage; but immediately after the formation of the ulcers, septic infection takes place, and secondary inflammation is set up in the mucosa. In such cases, the edges of the fistulous openings become inflamed, angry and œdematous, and sections through the margins of the ulcers show that the superficial layers of the mucosa are closely packed with masses of lymphocytes, the epithelial structures being especially affected. The violence of the reaction is, however, at first limited in extent, and strictly localized; hyperæmia and infiltration, although intense around the edges, are but slightly marked at a short distance from the ulcer; and it is only in severe cases, and at a very advanced stage of the disease, that these catarrhal areas unite, and inflammation becomes general. Under the microscope, the epithelial cells are seen to be granular, disorganized, detached or loosely adherent, with marked nuclear degeneration; many of

them are replaced by mucous cysts ; whilst, not infrequently, they combine with secretions from the damaged membrane to form patches of amorphous diphtheritic exudate on the surface of the mucosa. With the progress of septic inflammation, complete disintegration takes place. The infiltrated margins break down, and the ulcer gradually widens, but enlargement of the opening is accompanied by further deep excavation, and there is little relative change in the shape of the cavity.

*Efforts at Repair.*—In spite of the virulence of the necrotic process, amoebic ulcers display a remarkable tendency to heal. Even the largest are seldom without some evidence of attempts at repair ; and, when drainage into the intestine is free, the cavities generally exhibit extraordinary recuperative vitality. Almost immediately after sloughing has taken place, red granulations may often be seen pushing up from the base of an ulcer, and filling the hollows beneath the margins with apparently healthy tissue. In such instances, the discharge of blood and serum is replaced by a copious secretion of laudable pus, and complete cicatrization seems to be within measurable distance.

The new granulations are, however, very unstable, and, although fibrotic in character, they break down readily. The formation of permanent structures is incompatible with the continued development of entamoebæ ; and unless their growth is arrested at the same time there can be no production of durable tissue. The clinical features of the disease are, indeed, dependent on this factor. With the sloughing of a necrotic patch, the submucosa is relieved of the presence of a large number of organisms, and when granulation takes place the disorder enters on a quiescent stage. Ultimately, those entamoebæ which remain develop in sufficient quantity to cause a relapse ; and, as new tissue is especially liable to attack, recurrence of the symptoms is, almost invariably, due to its destruc-



tion. The condition of the colon in such cases—the commonest form of amœbic dysentery—is, consequently, one of continued cicatricial formation, alternating with the death of the newly-formed granulations.

### CHRONIC AMŒBIC DYSENTERY.

After repeated relapses the intestine assumes an appearance characteristic of lengthened infection. In large portions of the colon, the ulcers heal, infiltration is absorbed, and all traces of inflammation disappear. The new granulation tissue undergoes a fibrotic change; and the excess of connective tissue obliterates and replaces the normal structures. In severe cases in which a cure has been effected, the intestinal walls may be almost homogeneous. They become pale, thin, and parchment-like; the mucous membrane is bare and structureless; cicatrices and slate-coloured patches—the remains of extravasation—are scattered over its surface, whilst the epithelial glands are almost entirely absent. On section, the bowel is tough, dry, and leathery; at certain places it is thicker than at others, and this unequal development of connective tissue is followed by marked variations in the calibre of the tube. An extreme degree of contraction and obstruction, with subsequent dilatation above the strictures, is a frequent result of prolonged amœbic dysentery.

Seldom, however, is the process of fibrotic atrophy typical or complete; and alternating patches of fibrosis, persistent local inflammation, and suppurative ulceration due to continued development of *entamœbæ* are a more frequent *post-mortem* appearance. At some points the colon, which may be otherwise fairly normal, remains engorged, hypertrophied, and disintegrated; ulcers with fringed and undermined edges alternate with slate-coloured and fibrosed patches; and suppurating buttons of adenoid tissue may

be seen in close proximity to keloid scars and areas of devitalized and homogeneous mucosa.

#### PERFORATION OF THE INTESTINE.

As a rule, the base of an amoebic ulcer rests on the circular muscular fibres, and tissue destruction seldom extends beyond the submucosa. In ordinary circumstances, the opposition to the passage of pus which is naturally offered by the external walls of



FIG. 25.—Section of small amoebic abscess, in which the pus pushed through the muscular tissue, and collected beneath the serous coat of the peritoneum.  $\times 85$ .

the intestine is much greater than the resistance of the mucosa, but it occasionally happens that the muscular coat is invaded; and, when the peritoneum is weakened by infiltration and effusion, perforation may take place.

Although this grave complication sometimes occurs at the base

of an ulcer following coagulation necrosis, it is more frequently seen as a result of suppurative burrowing. When there is unusual tension in a submucous abscess, it may point downwards as well as upwards; and sections are not infrequently seen in which the pus, as if endeavouring to find an exit in both directions, has thrust aside the dense bundles of muscular fibres and reached the serous covering of the bowel.

In advanced amœbic dysentery of ordinary severity, one or two ulcers in this condition are almost invariably to be found; and it is, indeed, a matter for surprise that rupture does not occur oftener. The comparative rarity of the accident is due to the strength of the serous coat, and to the fortunate circumstance that in amœbic infections inflammation is of an unusually plastic and adhesive type. When there is deep ulceration, the omentum, the colon, and other structures are generally closely matted together, and the peritoneum is thus enabled to maintain the integrity of the intestinal tube.

*Localization of Lesions.*—In about 60 per cent. of all cases of fatal amœbic dysentery, the whole length of the great intestine is affected, the morbid process being usually most intense in the lower part of the bowel. If statistics are to be believed, however, there is considerable geographical variation in the extent to which particular sections of the alimentary canal are liable to attack. In the East Indies, the lesions are confined to the descending colon and sigmoid flexure in about 25 per cent of all instances, but in STRONG and MUSGRAVE'S first series<sup>3</sup> of 100 autopsies in the Philippine Islands, limitation of the disease to these areas was never once observed; whilst in their second series it was found

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<sup>3</sup> "The Pathology of Intestinal Amœbiasis." Reports of the Bureau of Government Laboratories, Manila, 1905.

only nine times. HARRIS states<sup>4</sup> that in America the lesions rarely extend above the hepatic flexure of the colon, although, in Calcutta, ROGERS<sup>5</sup> finds that they are almost invariably more marked in the cæcum and ascending colon, and that they are frequently limited to these areas.

The transverse colon is alone affected in only one out of every hundred cases of amœbic dysentery. Ulcers are occasionally seen in the lower part of the ileum, but lesions of the upper segments of the small intestine are very rare. WOOLLEY and MUSGRAVE<sup>6</sup> found the appendix involved in 15 out of 200 cases.

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<sup>4</sup> Harris, *American Journal of Medical Science*, 1898, p. 384.

<sup>5</sup> Rogers, *Brit. Med. Journ.*, 1903, No. 1, 1315.

<sup>6</sup> Woolley and Musgrave, "Reports to the Bureau of Government Laboratories," Manila, June, 1905.

## CHAPTER XIII.

THE CASE FOR THE PATHOGENICITY OF *ENTAMÆBA*  
*HISTOLYTICA*.

THE case for the specific nature of amœbic dysentery and the pathogenic function of *Entamæba histolytica* is based on observations and experiments, many of which have been already described. The pathology of the disease is, however, entirely dependent on the admission of these and other data as proofs, and, although a critical examination of the whole of the evidence entails some repetition, a certain amount of recapitulation is unavoidable.

Briefly, the argument for pathogenicity is fourfold :—

(1) There is a definite relation between the occurrence of the disorder known as amœbic dysentery and the presence of the organism. In every case *Entamæba histolytica* may be found in direct association with the prominent symptoms, discharges, and lesions, and the parasite is closely connected with the development of hepatic abscess—one of the most important complications of the disease.

(2) It has been shown that amœbic dysentery may be directly transmitted from one individual to another, and there is good reason to believe that infection is invariably conveyed by the agency of *Entamæba histolytica*.

(3) The lesions consequent on infection by *Entamæba histolytica* are of a constant and characteristic type, and they are widely

differentiated from those which are found in bacillary dysentery and in all other intestinal affections.

(4) If certain conditions are observed, an identical disease can be communicated to animals by infecting them *per os*, or by rectal inoculation, with material in which *Entamæba histolytica* is present. When the specific organism is not contained in the material no infection follows.

THE CASE AGAINST PATHOGENICITY.—Before dealing with these propositions in detail, it would be well to reconsider the arguments which have been advanced to show that amœbic dysentery does not originate in entamœbic infection, or, rather, that there is no evidence which warrants the differentiation of that disease from other types of dysentery. Shortly stated, they are :—

(1) That entamœbæ are often found in the dejecta of healthy persons, and in those of patients who are suffering from diseases other than dysentery.

(2) That direct infection has not been proved.

(3) That *Entamæba histolytica* has not been grown in pure culture, and that there is therefore no direct or conclusive evidence of pathogenicity.

(4) That deductions based on infection experiments on cats and other domestic animals are unreliable, on account of their natural predisposition to dysenteric affections.

(5) Finally, that the discovery of entamœbæ in the dejecta and lesions of dysentery is explained by natural and ubiquitous development of a normal inhabitant of the intestine, and that the organism has nothing to do with the production of the lesions.

(1) *Entamæbæ as Parasites of Healthy Persons*.—That amœbic organisms are frequently parasitic in the healthy alimentary canal is fully established, and recent research carried out in many different centres has shown (1) that infection by harmless entamœbæ



is fairly common all over the world, and (2) that there is a remarkable variation in the percentage of persons thus affected.

In Northern Europe, SCHUBERG found entamœbæ in 50 per cent. of the healthy population, a similar prevalence being recorded during the following year in Italy by KRUSE and PASQUALE. SCHAUDINN's figures for East Prussia agree closely with those of SCHUBERG, for, of sixty-eight healthy persons examined by him in that district, thirty-four harboured entamœbæ; whilst, at Rovigno, he found no fewer than 66 per cent. of the population affected. In France and Great Britain, infection by harmless entamœbæ, although much less frequent, is still fairly common; whilst in America, CRAIG, DOCK, and many other observers have repeatedly reported the great and undoubted frequency of *Entamoeba coli* as an intestinal parasite both in the North and the South of the Union.

In temperate climates, indeed, the endemic index is often as high or higher than it is in the tropics. In Manila, STRONG and MUSGRAVE found non-pathogenic entamœba in no more than 4 per cent. of the normal population. In Malaya, infection is, probably, somewhat more common; for in a series of cases of slight illness, mostly non-malarial febricula occurring in European and native patients of the better class, dejecta passed after a saline purgè were found by the writer to contain entamœbæ in 10 per cent. of all instances.

Many authorities, however, claim that not only is there a distinct relationship between non-pathogenic and pathogenic entamœbic infections, but that they are in fact the same; and they further suggest that harmless entamœbæ, probably by environment and lengthened residence in the alimentary tract, acquire new morphological characters and definite pathological functions. In support of this view, MUSGRAVE adduces the results of observations made on 300 prisoners in Manila jail, in which it was found that

101 of them harboured entamœbæ. Of these sixty-one were actually suffering from dysentery, but the other forty were quite well. Of the latter, however, eight died within two months, amœbic lesions being found in all of them; two were discharged from prison without further investigation; and of the remaining thirty, all developed amœbic dysentery within three and a half months.

But these results are by no means constant. All observers who have differentiated *Entamœba histolytica* from *Entamœba coli* are unanimous in declaring that the latter parasite is invariably innocuous, and it is at least significant that of the above series of cases examined by the author in Malaya, none afterwards developed dysentery.

Further, there does not appear to be any proportional relation between the endemic index of non-pathogenic amœbic infection and the case-incidence of amœbic dysentery. In countries where that disease is one of the most common affections, the percentage of people who harbour harmless entamœbæ is not so great as it is in places where the disorder is practically unknown. Thus, in Egypt, KRUSE and PASQUALE found entamœbæ only in two out of thirty-five healthy individuals—a result not dissimilar to that of STRONG and MUSGRAVE in Manila.

These statistics are unfavourable to MUSGRAVE's theory, but his observations are a striking illustration of the exceptional frequency of amœbic dysentery in Manila, and of the clinical fact that, in the earlier stages of the disorder, symptoms may be almost entirely absent. No deduction incompatible with Schaudinn's differentiation of species can be made from his work, or from any other statistical inquiry which has been reported. Even when influences, such as confinement, diet, and possible infectivity are left out of consideration, epidemic occurrences of amœbic dysentery can be better explained by a dual theory of entamœbic infection than

by any other. MUSGRAVE'S own observations, indeed, seem to support that conclusion ; and there is practically no other reasonable explanation of the fact that entamœbæ may be parasitic in the human intestine for very long periods without giving rise to dysentery, or to any symptom indicative of their presence. Immunity can be reasonably explained only by admitting the accuracy of the contention that in these cases infection is by a species which is essentially non-pathogenic.

#### FURTHER EVIDENCE.

The remaining arguments on both sides—based as they are on observation of the same phenomena and sequences of amœbic infection—may be considered together.

(2) *Infectivity of Amœbic Dysentery.*—Although the transmission of amœbic dysentery from a patient to a healthy individual, or from one patient to another in the ward of a hospital, cannot be regarded as conclusive evidence, the fact that infection frequently occurs in that manner, and that the organism is found in the dejecta of persons to whom the disease has been transmitted, affords considerable support to the case for the pathogenicity of *Entamœba histolytica*.

In the tropics direct infection is undoubtedly much more frequent than is commonly supposed, and most physicians are familiar with cases in which amœbic dysentery has been communicated by patients to other members of the family, to nurses, and to persons in attendance on the sick. It is, moreover, by no means unusual to find that in barracks, jails, and general hospitals, a case of amœbic dysentery acts as a focus of infection, and that patients in adjacent beds are attacked by the disorder.

In endemic areas, the importance of direct contagion has

naturally been underrated, and extension has generally been attributed to a common cause. Infection, however, occurs when the possibility of transmission from other sources is excluded; and many cases have been recorded in which patients returning from the tropics have communicated the disease to persons who could not have contracted it from the same source.

At a meeting of the Société Médicale des Hôpitaux de Paris, on October 28, 1904, Professor Dopter, of Val-de-Grâce, strongly emphasized the necessity of care in this respect, and brought forward instances of five soldiers who had never been abroad, but who acquired genuine amœbic dysentery from comrades who had become infected in the tropics. In one case an invalid soldier who had recently returned from Cochín-China suffering from amœbic dysentery, and who had a severe relapse while in barracks, communicated the disease to a recruit who had never been out of France, but who slept in an adjoining bed in the barrack dormitory. Microscopic examination of the dejecta revealed the presence of large numbers of organisms which had all the characteristics of *Entamœba histolytica*, and which contained many red blood-corpuscles. Search for the SHIGA-KRUSE bacillus and the results of agglutination reactions were negative; whilst, by rectal inoculation of a young cat, typical amœbic dysentery was reproduced, and in sections of the large intestine numerous entamœbæ were found in the tissues and in the glands of Lieberkühn. Proof of direct infection was, in short, complete; and the disease was no doubt transmitted by cysts, which were carried by flies to food or water consumed by the patient. As other sources of infection were excluded, the conclusion that in this instance a specific disease was conveyed by a specific organism is a reasonable deduction.

(3) *Cultivation Experiments.*—It has already been seen that no evidence material to the issue of pathogenicity has so far been fur-

nished by cultivation experiments. In the case of many pathogenic protozoa the difficulties of artificial culture have proved insuperable, and specific function has been established solely on the ground of constant association of an organism with the clinical condition, and with a definite pathological effect. To a great extent, this is also true of *Entamæba histolytica*; but, in this instance, the possibilities are more hopeful, for, although it has not been found practicable to satisfy the whole of the postulates formulated by KOCH for bacterial infections, *Entamæba histolytica* has undoubtedly been cultivated. On the other hand, it is more than questionable whether true amœbic dysentery has ever been transmitted by a pure culture, and it is doubtful whether a genuine infection can be reproduced by a culture of *Entamæba histolytica* in symbiosis with another organism.

The experiments which have been undertaken to determine the influence of symbiosis have done little to explain the phenomenon, and the results are, indeed, extremely perplexing. It has been supposed that the symbiotic bacteria might be the specific cause of the disease; but, so far as is known, every bacterium which is to be found in the dejecta of amœbic dysentery has been isolated and tested. Alone, most of them have been found to be innocuous, and none pathogenic. STRONG has suggested that symbiotic bacteria prepare the intestinal mucous membrane for invasion by entamœbæ, but his own experiment, in which he induced amœbic dysentery by tissue from sterile liver abscess, negatives the assumption that preparation is necessary; whilst JÜRGENS and RUGE have shown that entamœbæ may penetrate the mucosa without the aid of any variety of bacterium.

That symbiosis is not essential to the life and development of *Entamæba histolytica* is shown by the growth of the organisms in sterile hepatic abscess tissue, and it is probable that symbiosis is



necessary only when something else is absent from the environment. FROSCH'S law, indeed, still holds good. It is, that all varieties of amœbæ, free-living as well as parasitic, require for their development, natural or artificial, a special form of nutriment, which must be supplied either by the medium on which they grow or by a concomitant culture of bacteria.

*Entamæba coli*, moreover, has never been artificially cultivated, either pure or in symbiosis, and until this can be done, and the results compared with the effects of cultures of *Entamæba histolytica* on susceptible animals, an important link in the chain of evidence is missing.

(4) *Infection Experiments*.—Numerous investigators have shown that the vitality of many amœbæ, both free-living and parasitic, is unaffected by their artificial introduction into the lower intestine of certain animals, and it has also been proved that, conditions being favourable, these organisms continue to develop there, to multiply by schizogony, and when mature to encyst and pass out of the bowel with the fæces of their host. It has also been shown that the artificial transplantation of *Entamæba histolytica* into the rectum of a healthy cat, a dog, or monkey is followed by reactive inflammation, ulceration and other characteristic evidences of true amœbic dysentery, and that the introduction of *Entamæba coli* results only in an increase of the number of the organisms and fails to produce any symptoms of disease. Further, it has been ascertained that the administration, *per os*, of dysenteric dejecta which contain living entamœbæ is without effect, but that, if cystic forms are present in the material, development takes place in the intestine. In the case of *Entamæba histolytica* infection by the mouth is followed by dysentery.

These inoculation experiments, however, are by no means always successful, and in the case of *Entamæba histolytica* failure is the



rule rather than the exception. It may be due to the absence of viable organisms from the experimental material, but more often it is caused by lack of susceptibility, or by unsuitable conditions in the alimentary canal of the host. Acidity is, for instance, highly unfavourable to the growth of protozoa, and *entamœbæ*, placed in an acid medium, perish almost at once. Susceptibility besides decreases rapidly with age—a peculiarity which is specially noticeable in certain animals; thus, young cats are readily infected, whilst old cats are often extremely resistant.

Natural predisposition also varies greatly. Most of the domestic animals generally utilized for experimental purposes are naturally predisposed to dysentery, and cats are so prone to this form of intestinal disease that the significance of experimental infection in these animals has often been questioned. It is indeed the case that, unless the results are carefully tested and compared with controls, experiment is useless; for as reactive inflammation with dysenteric symptoms may follow the injection into young cats of almost any irritant, it would be unjustifiable to assume that amœbic dysentery had been successfully transmitted unless, after a certain lapse of time, *Entamœba histolytica* could be demonstrated in the dejecta.

Again, the type of disease experimentally induced in cats is generally of greater intensity than the clinical condition which is seen in man. Not only do these animals react more freely to mechanical irritation, but they are apparently more susceptible to the influence of the toxins produced by the development of the parasites; and the injection of *Entamœba histolytica* is often followed in cats by collapse, paralysis, and fatal toxæmic symptoms before dysentery is fully established.

That the condition is true amœbic dysentery there can, however, be no doubt. The insignificance of the morbid changes so fre-

quently noted when the constitutional symptoms have been most intense is due to the fact that the animal is killed by the toxin before the stage of ulceration is reached ; when it survives the first effects of the poison typical ulcers are always produced. Even in the earliest period of infection in cats, characteristic infiltration of the submucosa and lymph follicles is noticeable, and *Entamæba histolytica* can almost invariably be demonstrated in association with all the lesions.

Further striking and conclusive evidence of the pathogenicity of *Entamæba histolytica* is supplied by the general morbid anatomy and histology of the experimental lesions in animals. If a cat, to which amœbic dysentery has been successfully transmitted by rectal inoculation, is killed three days after the injection, the mucosa of the colon will be found to be swollen, infiltrated, and discoloured by submucous hæmorrhage. A day or two later, the results of inflammatory reaction are still more apparent ; points of necrosis appear, and on the intensely congested membrane small ulcers, sometimes so minute as to be almost invisible, make their appearance. At a more advanced stage the ulcers increase in size and depth, and their edges, which are surrounded by an angry areola, are seen to be irregular and deeply undermined. In some cases, necrosis now becomes general ; the unbroken surface gives way, and the scattered sores coalesce to form large ulcerated patches extending down to the muscular coats. At a still later period, the upper layers are completely shed, the muscle being then entirely denuded, or covered only by ragged fringes of disintegrated mucous membrane. This wholesale destruction is generally limited to the sigmoid and lower bowel, but the upper part of the colon is often affected, and the lymph follicles and vessels throughout the entire length of the great intestine are congested and engorged. The mesenteric glands are also infiltrated and swollen.

Microscopic examination of the tissues shows that these morbid changes are, invariably, of a characteristic amœbic type. In cases of irritative inflammation and in the bacillary variety of dysentery, reaction commences in the superficial layers ; but, in amœbic infections in cats, as in man, the initial process always occurs in the submucosa. In fresh sections (which should be cut with a warm knife and kept moist by saline solution), the movements of the entamœbæ in the tissues can be watched for three or four hours ; and, by this method, the points which are first selected for attack and the route taken by the invading organisms may be clearly traced.

If two sections of intestine are made, one through an ulcerated patch, and the other through inflamed but unbroken mucosa beyond its undermined edge, entamœbæ will be found in both of them ; but whilst in the case of ulcers it is impossible to say whether the organisms are a secondary infection on tissue already necrosed and broken down, the appearance of the deeper layers below an intact surface is so characteristic that the rôle of the entamœbæ in producing these changes can scarcely be doubted.

As in man, the usual route of invasion is by Lieberkühn's glands ; and, in the earliest stage of infection, entamœbæ may often be seen lying free in the lumen of these tubes, the epithelium being, as yet, intact and unchanged. At a slightly later period, the organisms push in between the epithelial cells at the fundus of the gland ; and most of these, in consequence, degenerate and become hazy and granular. On reaching the basement membrane the entamœbæ collect in groups on its epithelial aspect, but soon afterwards they traverse it and spread out into layers on both sides of that structure. Here they rest for some time, and, apart from the detachment and destruction of the epithelium caused by the parasites, they apparently give rise to little reaction. Ultimately, however, as they

increase in numbers, they push out in all directions from the base of the gland, wedging themselves by a succession of powerful movements into the meshes of the connective tissue, and tearing asunder the bundles of fibres. With their extension into the submucosa a copious transmigration of small cells takes place round them, and necrotic areas form along their tracks where the infiltra-

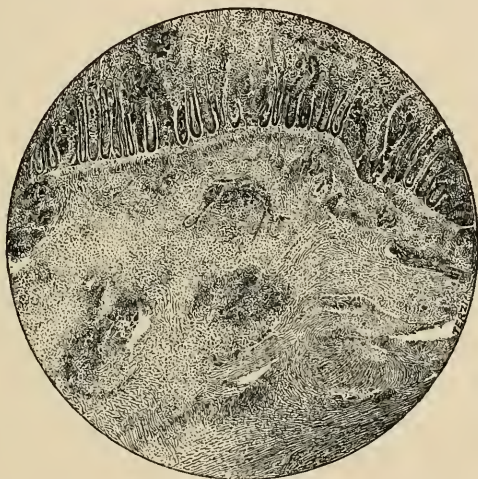


FIG. 26.—Section of experimentally infected cat's colon. The glands of Lieberkühn are full of entamoebæ, which are scarcely visible by this magnification. Dense infiltration of the submucosa, with incipient abscess formation, is seen to be due to lateral, not superficial, invasion.  $\times 55$ . (After Jürgens.)

tion is most intense. These points are often at a considerable distance from the Lieberkühn's glands, and the mucosa overlying them is at first quite healthy. Subsequently, it becomes inflamed and gangrenous ; but as the surface breaks down it can be seen that the process is a secondary one, that it does not commence from above, and that it is due to strangulation of the blood-vessels and lymphatics by a mass of infiltrated cells.

The influence of the entamœbæ in the production of these changes can be followed step by step. The lesions at every stage are clearly secondary to, and dependent on, the invasion of the submucosa by the organisms; and the consequences which result from the migrations and destructive influence of the parasites widely differentiate amœbic dysentery from all other intestinal diseases.



FIG. 27.—Experimentally infected cat's colon. (The section is the same as that shown in fig. 25.) Under the higher magnification, the glands of Lieberkühn are seen to be full of entamœbæ, which have destroyed most of the epithelium, and are traversing the basement membrana.  $\times 350$ . (After Jürgens.)

*Feeding Experiments.*—Almost every observer since LÖSCH, has endeavoured to communicate amœbic dysentery to animals by mixing small quantities of dysenteric material with their food; and in a certain proportion of these experiments characteristic symptoms have been successfully reproduced. It has also been found that, in the case of cats, dogs, and monkeys, the period of



incubation is usually about four days; and that at the end of that time *Entamæba histolytica* may generally be demonstrated in the dejecta of the experimental animal. Moreover, it has been shown that in cats infection by the mouth is followed by symptoms which, although generally less acute than those produced by direct transplantation of dysenteric material into the rectum, are still considerably more serious than those characteristic of the clinical condition seen in man, and that the acute toxic or fulminating type is by no means uncommon.

Like many other pathological tests, feeding experiments are apt to prove fallacious, and unwarranted deductions may easily be drawn from them. It is, for instance, obvious that before a claim to pathogenicity can be substantiated the material used must be shown to be free from organisms, such as SHIGA'S bacillus, or other substances which might themselves cause dysentery; and further, that if the specific nature of *Entamæba histolytica* is to be established, the absence of *Entamæba coli* must also be demonstrated.

In the earlier experiments, these conditions were unaccountably disregarded. Inadmissible conclusions were in many instances based on results which in themselves proved nothing; and capable investigators committed themselves to statements of belief in the pathogenicity of the organisms upon data which, had they been dealing with another disease, they would have summarily rejected. As other potential causes of dysentery were left out of account, few, if any, of these experiments possess the slightest value; and much of the incredulity with which the original claims for pathogenicity were received was directly due to this inexactitude.

Recent investigations, however, show that important information may be obtained from feeding experiments, if they are carefully conducted. SCHAUDINN endeavoured to exclude possible sources of error in the following way: From a case of chronic amœbic dysent-



ery contracted in China, in which the absence of SHIGA'S bacillus had been proved, a specimen of dejecta was collected and divided into three portions. In order to induce encystment of the living entamœbæ, these portions were evenly spread in thin layers on slides, and dried in the air. After some time the smears were freely moistened with water, and cover-glasses were applied, so that, by means of a mechanical stage, every part of the preparation could be systematically searched. In this way, some twenty specimens, in which encystment was complete, were thoroughly examined; and no cysts of *Entamœba coli* or other organisms having been found, SCHAUDINN considered himself justified in concluding that the only forms of amœbic life contained in the dejecta were the cysts of *Entamœba histolytica*, which, of course, were present in great abundance.

Ten *coli*-free specimens were thereupon selected, and the cover-glasses having been removed, the smears were carefully rubbed up with distilled water to make a volume of 1 c.c. This was administered, with a meal of meat and milk, to a healthy young cat (cat A), the dejecta of which had previously been proved to be free from amœbic organisms and cysts. On the evening of the third day, the cat was seized with acute dysentery, and died the following afternoon, having in the meantime passed a large quantity of mucus and blood, in which were many typical and active specimens of *Entamœba histolytica*. Sections of the intestine revealed a characteristic dysenteric infiltration necrosis, the morbid changes being exactly similar to those produced in cats by rectal injection of fresh dysenteric dejecta.

In order, further, to determine whether fresh excreta which contained no cysts, but only active forms of *Entamœba histolytica*, were pathogenic when administered by the mouth, SCHAUDINN fed another healthy cat (cat B) with the dejecta of cat A. These were

known to contain no cysts, as, apart from the fact that there had been insufficient time for encystment to take place, their absence had been demonstrated by an exhaustive search of the intestinal contents. The dejecta of cat B were examined daily for four weeks without result ; no entamœbæ were found, and the animal remained perfectly well.

A second portion of the dried dejecta from the case of Chinese dysentery—known to contain cysts only—by which cat A had originally been infected, was now given to cat B, with the result that, in six days, *Entamœba histolytica* appeared in the dejecta, and, within a fortnight, the animal died after a typical attack of amœbic enteritis.

SCHAUDINN'S experiments may be regarded as conclusive so far as they establish the dual nature of entamœbic infection, the pathogenicity of *Entamœba histolytica*, and the method in which transmission usually takes place ; but they do not altogether exclude the possibility of the disease being due to some other agency, infection by which may, conceivably, be a necessary preliminary to subsequent invasion by entamœbæ of its lesions. Until the disease is reproduced by the pathogenic organism in pure artificial culture, that assumption cannot be finally refuted ; and SCHAUDINN, who was himself unable to cultivate *Entamœba histolytica*, fully admitted the strength of the objection.

The possibility of error from this source had, however, been previously reduced to a minimum by the observations of KARTULIS and KRUSE and PASQUALE in Egypt, and more especially by the experiments of STRONG in Manila. KARTULIS had shown that, in many cases of hepatic abscess, the pus, although it contained living amœbæ, was otherwise sterile ; and he, therefore, concluded that, if by its means amœbic dysentery could be transmitted to healthy animals, the element of doubt as to concomitant bacterial infection

would be eliminated. This he was able to do, and KRUSE and PASQUALE repeated and definitely confirmed his experiments.

The question of the infectivity of sterile hepatic pus, however, remained in a somewhat unsatisfactory position; and objectors to the doctrine of pathogenicity contended that the results obtained by KARTULIS were inaccurate, and that although ulcerative colitis was produced, and although amœbæ were found in the intestinal contents, the lesions were unlike those of amœbic dysentery, and the type of illness was so dissimilar that it indicated a septicæmic reaction to the products of disintegrating tissue rather than a true amœbic infection. These and other difficulties were, however, finally settled by STRONG, who showed that previous experiments had been vitiated by the fact that an excessive quantity of pus had been injected; and, using only carefully selected material from the walls of abscesses, he was able to prove that typical symptoms and morbid changes were invariably induced in cats by the injection of sterile hepatic pus. STRONG's specimens and preparations, which are now in the museum of the Army Medical Department at Washington, afford one of the most complete proofs of the essentially protozoan character of amœbic dysentery.

PART V.—ETIOLOGICAL.



## CHAPTER XIV.

## THE CAUSES OF AMŒBIC DYSENTERY.

*General Predisposing Influences.*

*The Influence of Age.*—Amœbic dysentery occurs at all periods of life, and if opportunity for contracting the disorder is taken into account, liability to infection is approximately the same at all ages.

The disease is by no means uncommon in young children. LAMBL'S original observation was made on a child two years of age, and recent writers have reported numerous instances in infants. In a careful study<sup>1</sup> of five cases of amœbic dysentery which were treated in the children's ward of the Johns Hopkins Dispensary, Baltimore, AMBERG gives the ages of his patients as 3, 5, 5, 2½, and 4 years respectively; and KARTULIS states that in Egypt amœbic dysentery occurs almost with equal frequency at all periods of life. In the Malay Peninsula, pathogenic amœbæ have been repeatedly found by the writer and other observers in cases of infantile dysentery; and one instance of undoubted infection by *Entamœba histolytica* was seen in a Chinese baby of ten months, which was stated to be exclusively breast-fed. The age of a patient, whose case is fully reported by CAHEN,<sup>3</sup> was 4 years, and GNEFTOS has recorded<sup>4</sup> a copious infection of amœbæ in pus taken from the liver of a boy of 7.

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<sup>1</sup> Amberg, S. A., *Johns Hopkins Med. Bulletin*, 1901, p. 355.

<sup>2</sup> Kartulis, *Die Protozoen als Krankheitserreger*, Jena, 1891.

<sup>3</sup> Cahen, *Deutsch Medicin. Wochenschrift*, 1891, p. 853.

<sup>4</sup> Gneftos, *Deutsch Medicin. Wochenschrift*, 1900, p. 515.



Hepatic suppuration of any kind is, however, very rare in children, and when it occurs it is generally of traumatic origin. Personally, I have seen only one instance of abscess of the liver before the age of 10. In that case—a European girl, 8 years old, who had never been out of the tropics—there was a doubtful history of dysentery, but a definite statement as to an injury two months before. Amœbæ were found in abundance in a large abscess which was opened below the costal margin. This exceptional immunity of young subjects applies to other countries, for AMBERG states that a careful search of all the American records resulted in the discovery of no more than eleven cases of hepatic abscess in children less than 7 years old.

In amœbic dysentery the ratio of incidence increases rapidly with adolescence. In FUTCHER'S series of 119 cases, treated at the Johns Hopkins Hospital, 34 were under twenty, and 65 contracted their illness between the ages of twenty and thirty. STRONG'S analysis of 200 cases investigated by him in the Philippines shows that the disease developed in 149 of the patients when they were between twenty and forty. In Malaya, the average age of 50 per cent. of the patients treated is from twenty to thirty, and in the Andaman Islands the preferential period of life is approximately the same. After forty, the case incidence everywhere falls rapidly.

Statistics, however, render little assistance in determining the actual predisposition to amœbic dysentery at different ages. Except in the case of the Naval and Military Services, and in institutions, such as jails, convict settlements, &c., it is difficult to obtain accurate figures, and even in these returns the results are vitiated by the fact that troops and the inmates of penal settlements are mostly young adults. Records of the incidence of amœbic disease which have been compiled in the tropics seldom take into account the average age of the general population, or the opportunities which

the patients have had of contracting the disease; and, as indicative of age incidence, they are, in consequence, of little value. It is mostly between the ages of twenty and forty that men are exposed to the vicissitudes of military service, jungle work, and outdoor life generally, and the risks of infection are consequently greater at that time than at any other time. Variations in age incidence are, in short, due rather to the opportunities of infection than to the period of life.

*The Influence of Sex.*—For the same reason, the records of sex incidence cannot be regarded as expressing any actual sex preference. It is true that the vast majority of patients are males, but this, again, is doubtless due to the fact that men are more exposed to infection than women. In FUTCHER'S series of 119 cases, to which allusion has already been made, 108 were males, and 11 only were females. Of STRONG'S 200 patients, no fewer than 177 were men; and returns compiled in the Government hospitals and in private practice in the Eastern tropics show that five males to one female is an average proportion. There is, however, again no question of comparative predisposition. Both sexes acquire the disease with equal facility; and the experience of most tropical physicians is that European women and girls are specially liable to infection.

*Race Predisposition.*—Similarly, there is no reliable evidence that one race shows greater inherent susceptibility to infection than another. It is held by many authorities that Europeans are exceptionally prone to amœbic disease; but it is certainly true, as BALFOUR pointed out many years ago, that relatively to population the case incidence of all varieties of dysentery is much higher in native races. BUCHANAN and others have shown that in India native soldiers are far more liable to dysentery than white troops who are stationed in adjacent cantonments; and in the West

Indies the proportion of admissions to the military hospitals is as 26 non-Europeans to 11 white soldiers.

For an explanation of these statistics, there is, however, no necessity to go beyond the hygienic conditions by which the respective communities are surrounded. When Europeans live in filthy houses, when they eat bad or carelessly prepared food, when they drink polluted water, when, in fact, they expose themselves to infection in the same way, they acquire amœbic and bacillary dysentery in exactly the same ratio as black, brown, or yellow men in similar circumstances. Moreover, the predisposition of the various native races corresponds accurately to their habits of life. The better classes of the Chinese residents in British Malaya invariably drink hot water or weak tea, and refuse to touch water which has not been boiled, and they are, in consequence, but little affected by amœbic dysentery. One or two castes of Hindoos follow the same practice, and secure a like exemption; but other communities who are less careful in their habits suffer severely.

*Climatic and Meteorological Influences.*—No characteristic of amœbic dysentery has been more fully attested than the influence which is exercised on the endemic prevalence of the disease by excessive moisture and floods. COUNCILMAN and LAFLEUR, in their original paper, called attention to the frequency of amœbic dysentery in the wet and swampy districts of America, and instanced the Mississippi Valley and the low-lying country round Chesapeake Bay as special centres of infection. In Egypt, the intimate relation between the frequent occurrence of the disease and the annual overflow of the Nile has been pointed out by numerous observers; and the persistent prevalence of amœbic dysentery in the riverine alluvial flats and deltas of the Eastern tropics is notorious.

In India and the Malay Peninsula the period of greatest prevalence is generally coincident with the floods at the break of the

monsoons. The connection between a heavy and prolonged rainfall and the incidence of the disease is, indeed, remarkable. MUSGRAVE relates that after the great flood which occurred in Manila in 1904 amœbic dysentery assumed a type which was practically that of an epidemic, and states that the direct relation of excessive moisture to the frequency of the disease was undoubted.

The influence of floods in the causation of dysentery is readily intelligible. In the tropics, much filth and sewage which otherwise would be effectually sterilized by drought and sunshine are washed into the wells and watercourses at the beginning of the wet season, and heavy rain after drought invariably means increased pollution. No doubt it is in this way that moisture has come to be associated with the prevalence of amœbic dysentery, for it must be remembered that a damp soil is by no means essential to the existence of the disorder. It is endemic in many districts which are proverbial for aridity and drought; and KARTULIS and others have suggested that in Mecca and Arabia generally the frequency of amœbic dysentery is actually a result of the inadequacy of the water supply, and consequent liability of the wells to contamination.

*Seasonal Prevalence.*—Apart from the influence of excessive moisture, there is considerable difference of opinion as to seasonal prevalence. It is true that in the tropics amœbic dysentery is generally greatly in evidence during the cool season, but the apparent increase in the frequency of the disorder is due to the accentuation of the symptoms and the greater tendency to relapse, rather than to augmented infection. Infection, indeed, generally takes place during the hot and wet months, and there may be no prominent clinical effects until they are evoked by chill.

In Egypt, the period of greatest frequency is undoubtedly the late summer and autumn; and in Baltimore and other parts of America the incidence of amœbic dysentery accurately corresponds

with the mean atmospheric temperature. The same seasonal prevalence occurs in China, and, indeed, in most other subtropical countries; the curve beginning to rise in May, attaining the highest point in July or August, and falling rapidly after September. Reports from other places, however, indicate that there are exceptions to this law of periodic frequency. MARCHOUX, for instance, believes that amœbic dysentery is most prevalent in Senegal during the last quarter of the year, and most infrequent during the first; and ROGERS states that in Calcutta there is no variation in seasonal prevalence.

ACTUAL CAUSATION.—Although our knowledge of the cycle of events in the extra-corporeal life of *Entamœba histolytica* is incomplete, there is no doubt that the usual vehicle of infection is drinking water, and that contamination of food and water supplies by fæcal matter is the almost invariable cause of tropical dysentery. If it is agreed that amœbic disease is specific, that it originates in infection by a particular organism, and that it is not and cannot be conveyed by media which contain only free-living or non-pathogenic amœbæ, it follows that every instance of amœbic dysentery is traceable to a previous case of the disease.

There is abundant proof that water which contains only organic impurities, with the free-living amœbæ which feed on them, is powerless to induce amœbic dysentery; and that unless it is polluted by fæcal matter it may be consumed for long periods without obvious detriment. On several occasions I have found that drinking water on board sailing ships arriving at an Eastern port after a long tropical voyage contained large numbers of free-living amœbæ and other organisms, but although it had formed the sole supply of the crew for three or four months there had been during that time little illness and no intestinal derangements. Rain water collected and stored in tanks in the tropics almost invariably swarms with



amœbæ ; but it seldom gives rise to internal trouble, and never, unless contaminated, to specific dysentery.

On the other hand, provided that *Entamœba histolytica* in the encysted condition is present, even in imperceptible numbers, amœbic dysentery may be conveyed by the clearest and most wholesome-looking water. PLEHN and other writers have repeatedly pointed out that tropical dysentery is often most plentiful in settlements where the water supply is bright, clear, and sparkling ; and that in places where it is turbid and foul there are comparatively few cases.

The appearance of drinking water has, of course, no relation to its possible infectivity. In many tropical cities the supply is derived from surface rain water collected from catchment areas in the neighbouring hills, and it passes direct into the service pipes without storage in an impounding reservoir. During the first part of the rainy season the drinking water is, in consequence, always muddy and discoloured, and diarrhœa and dysentery are very prevalent. Amœbic dysentery, especially, can often be traced to infection at this season, and it is doubtless due to the fact that encysted organisms are washed into the water supply.

In the country districts, on the other hand, the water supply is usually taken from deep wells, and amœbic dysentery shows less variation in its seasonal incidence. Wells, however, are extremely liable to surface pollution, and unless carefully shut off from contamination may constitute permanent and continuous sources of infection.

If a catchment area can be maintained under jungle, and kept free from human habitation, it affords, perhaps, the safest method of collection ; but on the other hand, when liable to pollution, it is the most dangerous. When there is no opportunity for sedimentation, the contaminated water is borne direct to the consumer, and it thus escapes the purification which it undergoes in a settling tank,



where broods of protozoa and bacteria meet numerous natural enemies. In such circumstances, amœbæ of all varieties are exceptionally easy victims; and it is for this reason that river water is less likely to propagate amœbic dysentery than to convey cholera, bacillary dysentery, and other bacterial diseases in which the pathogenic agents are so small as to escape detection.

In the tropics also there are many other ways in which water-borne infection may be conveyed. Milk is often diluted from contaminated puddles or placed in vessels which have been washed in dirty water; improperly cleansed dishes, spoons and forks are fertile sources of infection; and green vegetables are generally manured by water in which large quantities of night-soil have been dissolved. In one case which came under observation, amœbic dysentery undoubtedly originated in the use of cold water enemas which had been recommended as a remedy for constipation. "Bazaar" aerated and sweet drinks are invariably prepared from unsterilized water, and some of them are indescribably filthy; whilst, in the encysted state, *Entamœba histolytica* without doubt survives enclosure in ice for considerable periods.

Moreover, it should not be forgotten that water may be contaminated from excess of precaution. A familiar instance of this occurs in the use of filters. A filter once infected is a perpetual source of danger until it is properly sterilized—an operation which requires considerable technical knowledge, and which can seldom be carried out at home. The sides of a "dripstone" or ordinary domestic filter in the tropics afford an unrivalled breeding-ground for amœbæ, and large numbers of free-living organisms may generally be collected from both surfaces of these vessels. Water which has been sterilized by boiling is thus frequently reinfected by subsequent filtration; and if a filter is used at all it should be employed to remove the sediment only before and never after the water is

boiled. Raw vegetables and uncooked green stuff also constitute a frequent source of infection. In the tropics, free-living amœbæ are found in abundance on lettuces, cucumbers, tomatoes, radishes, and the various herbs which are used for garnishing cold meat, &c. They are, besides, plentiful in table water, in milk, and on the meat itself ; and as they adhere closely—MUSGRAVE and CLEGG showed that five or six vigorous washings were insufficient to remove them from salads—the entrance of considerable numbers of these organisms, alive or encysted, into the alimentary canal is inevitable. Infection by the pathogenic species is doubtless effected in the same way when lettuces and other vegetables have been supplied with water or liquid manure contaminated by the specific organism.

In conclusion, there can be no doubt that, in the great majority of instances, amœbic dysentery is water-borne, and that infection is generally conveyed by organisms in an encysted condition. Doubtless many of them are destroyed by the gastric juice ; but in the resting condition *Entamœba histolytica* offers considerable resistance to fairly strong solutions of acid and other disinfectants, and an infinitesimal number of organisms may cause a serious attack. The gastric secretion may, moreover, be disordered and ineffective ; and in weak dilution, as in copious draughts of water, encysted and even living entamœbæ are likely to pass unaltered into the intestine.



PART VI.—THE COMPLICATIONS AND SEQUELÆ OF  
AMŒBIC DYSENTERY.



## CHAPTER XV.

## HEPATIC ABSCESS.

OF the graver complications of amœbic disease, abscess of the liver is, by far, the most frequent and the most fatal. Occurring especially as a sequela of dysentery acquired in the tropics, it is usually known as tropical abscess of the liver, but it is by no means uncommon in temperate climates, and it is occasionally seen in England. The condition may be briefly defined as suppurative hepatitis, induced through an invasion of the liver tissue by *Entamœba histolytica*.

*Historical Note.*—Since the time of Hippocrates, the connection between hepatic abscess and dysentery has been known to physicians, and the writings of the older anatomists contain many references to the frequency of the association. As a complication of camp dysentery—then, as now, the scourge of armies in the field—abscess of the liver was very prevalent in the seventeenth and eighteenth centuries, and, during the Seven Years' War, it was even more frequent in Europe than it now is in India. Sir JOHN PRINGLE, in his work on the Diseases of the British army in Flanders, which was published in 1752, states that abscess of the liver was the most common sequela of dysentery in the Low Countries, whilst the official reports of BLANE and other naval surgeons bear witness to a similar frequency of this complication in the British fleets.

The almost contemporary writings of JOHN HUNTER, who was



then in Jamaica, indicate the prevalence of liver abscess as a complication of the endemic dysentery of the Western tropics, and, in the report of his researches on the diseases of the West Indies, there is a graphic description of the morbid anatomy of "chronic flux," with a lucid statement of the pathological relations between ulceration of the colon and the formation of pus in the liver.

In the nineteenth century, a notable diminution took place in the prevalence of hepatic suppuration in Europe; and, although during that time there were many severe epidemics of dysentery, it was observed that liver abscess had become very rare. It was even suggested by BUDD and SYDENHAM that dysentery had altered in type or virulence, but as the disease itself was then more fatal than ever, and as liver abscess was reported to be still the most frequent complication of dysentery in the tropics, the belief became current that hepatic suppuration was indicative of malaria—then regarded as a climatic infection.

During the next few years, numerous *post-mortem* records and statistics of prevalence were accumulated in India by ANNESLEY, MOREHEAD, FAYRER, MACLEAN, and other observers; and in Cochin China and Algiers by DUTROLAU, JULLIEN, DELIOUX DE SAVIGNAC, and KELSCH and KIENER, but until the differentiation of amœbic dysentery from other varieties of the disease no advance was made on the malarial theory of origin. Soon after the publication of COUNCILMAN and LAFLEUR's article, however, the claim of these authors that hepatic abscess occurred only as a sequela of amœbic dysentery was generally endorsed by pathologists, and the researches of KARTULIS, BABES, KRUSE, PASQUALE, ZANCAROL, MUSGRAVE, and many other investigators fully attest the importance of that observation.

Some difficulties and anomalies—chiefly racial or geographical—remained for explanation. GRIESINGER, working in Egypt, had

reported that although hepatic suppuration was not uncommon among Europeans, in 186 autopsies on natives who had died of amœbic dysentery he had not seen a single instance. In India, although the complication was found in 34 per cent. of all whites who died of dysentery in the Government hospitals, abscess of the liver rarely occurred in natives, who were even more liable to dysentery than Europeans; and BUCHANAN afterwards showed<sup>1</sup> that the relative incidence of hepatic suppuration in India was approximately as follows:—

Liver abscess complicated dysentery (all grades of severity included)

In European troops	...	...	...	...	once in 18 cases.
In native troops	...	...	...	...	„ 355 „
In native civil prisoners	...	...	...	...	„ 681 „

It was apparent, however, that the predisposition of the white soldier and the comparative immunity of the native could not be attributed either to racial influence or to a difference in the type of dysentery by which they were attacked. FINGER, of Prague, had already shown that, in temperate climates, hepatic suppuration was now very rare, and that in a series of 150 autopsies on patients of all nationalities in that city who had died of amœbic dysentery there had been no instance of liver abscess. On this important point his evidence was confirmed by COUNCILMAN and CHIARI, the former of whom said:<sup>2</sup> “Material brought from Prague could be used as typical specimens to illustrate amœbic dysentery, yet we never saw a single case of liver abscess due to amœbæ.”

*Modern Views as to the Etiology of Hepatic Suppuration.*—Further researches by ROGERS, KARTULIS, JÜRGENS, VIERECK, MUSGRAVE, DOPTER, and others have disposed of most of those difficulties.

<sup>1</sup> W. J. Buchanan, *Journ. of Trop. Med.*, 1899, p. 173.

<sup>2</sup> Councilman and Lafleur, *Johns Hopkins Reports*, 1891.

Undue weight had undoubtedly been attached to difference in the geographical distribution of the two conditions; and most of the assertions which have been made as to the immunity from liver abscess of certain places, where amœbic dysentery is endemic, are now known to be inaccurate. It is, for instance, stated by many writers that in Kamerun, and in Singapore, dysentery is never followed by hepatic suppuration. The facts are<sup>3</sup> that all over German West Africa abscess of the liver is very common; and it is so frequent in Singapore, and throughout Malaya generally, that South-eastern Asia has come to be regarded as a special *foyer* of the complication.

The racial differences in the incidence of liver abscess have also been shown to depend rather on dissimilarity in the habits of life than on variations of the type of dysentery. Communities which are habitually abstemious suffer scarcely at all; and it is reasonable to suppose that their immunity is due to absence of tendency to hepatitis. Two conditions—and, practically, only two—are now regarded as essential to hepatic suppuration after dysentery:—

- (1) Predisposition, owing to alcoholism, excess, exposure, &c.
- (2) The implantation of *Entamoeba histolytica* in liver tissue.

This conclusion is further supported by the fact that liver abscess is comparatively rare in females, and that, as has been seen, it is very infrequent in young subjects. Recent arrivals in tropical climates are said to be more liable to hepatic suppuration than those who are acclimatized; but personal experience is directly opposed to this view, and I have been unable to find any reliable figures which support it. Length of residence appears to be a predisposing cause rather than otherwise.

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<sup>3</sup> See *Medizinal Berichte über Deutschen Schütz-gebiete* (1907-8), Kamerun, p. 174, &c.

*Evidence of the Amœbic Origin of Liver Abscess.*—Amœbic abscess of the liver is occasionally seen in animals as a result of natural infection, and it frequently follows experimental amœbic dysentery induced in cats, dogs and monkeys. STRONG reports a case in which an orang-utan in Manila developed a hepatic abscess after amœbic disease of the appendix ; and, in a report presented to the first Egyptian Medical Congress in 1904, mention is made of a badger which died at the Zoological Gardens in Cairo from dysentery with subsequent suppuration of the liver. In this case *Entamœba histolytica* was demonstrated in all the lesions.

In 75 per cent. of all cases of tropical abscess of the liver there is a distinct history of dysenteric symptoms ; and, as was shown by ZANCAROL, of Alexandria, and MACLEOD, of Shanghai, in almost every fatal instance in which a precedent attack of dysentery has been denied, amœbic lesions of the intestine, recent or healed, may be demonstrated after death. Including definite *post-mortem* evidence of amœbic infection of the colon, ROGERS found<sup>4</sup> that, in Calcutta, 95 per cent. of all cases had previously suffered from dysentery. MUSGRAVE also stated<sup>5</sup> that, in the Philippine Islands, more than that proportion of all liver abscesses were amœbic ; whilst a similar experience has been recorded by observers in China, in British and Dutch Malaya, and in other parts of the tropics.

ROGERS further showed that living entamœbæ were present in the walls of thirty-five out of a series of thirty-seven liver abscesses, and that, in the two cases in which they were not found, the cavities had been incised and drained twelve days before the tissues were examined. In two-thirds of these cases, the contents of the abscess were sterile, and entamœba was the only organism which was

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<sup>4</sup> L. Rogers, *Brit. Med. Journ.*, 1903, i., p. 1315.

<sup>5</sup> W. E. Musgrave, *Philippine Journal of Science*, June, 1906.

constantly associated with the condition. He also confirmed COUNCILMAN and LAFLEUR's original observation that, in most instances, focal centres of necrosis in the liver originate from thrombi in the smaller branches of the portal vein, and that living entamœbæ are generally entangled in the clot.

*Period of Development.*—Hepatic suppuration occurs almost at any time after amœbic infection. Cases are recorded by ANNESLEY and others in which it preceded the dysenteric symptoms, although that must be very rare; but pus sometimes develops in the liver within a week of the actual invasion of dysentery. In the great majority of instances, however, the complication is a late one, the first evidence of hepatitis being usually noted about the fifth or sixth week. When amœbic dysentery becomes latent or chronic, hepatic suppuration may appear months or years after the first attack. In one instance which came under personal observation, an amœbic abscess formed twelve years after the patient had left the tropics, and nine after his last dysenteric attack.

*Situation and Relations of Amœbic Abscesses.*—Although generally deeply embedded in the substance of the gland, an abscess cavity is seldom equally surrounded by liver tissue, and some part of the wall is usually in contact with the outer surface; the upper and posterior portion of the right lobe being the region which is most prone to suppuration. When an abscess forms in this situation, the thoracic limits of the liver are considerably altered, and the upper line of dulness is raised two or three inches by the bulging of the dome. In such cases, the tissues are generally so matted together by infiltration and pressure, that the capsule is softened and destroyed, and the adherent diaphragm constitutes the upper wall of the cavity. These subdiaphragmatic abscesses of the liver usually point close to the suspensory ligament, and, unless surgically treated, burst into the lung or pleural cavity.

Less frequently a large solitary abscess develops in the right lobe close to the ribs and points below the costal arch, with the formation of numerous adhesions to the omentum, colon and other viscera. The left lobe is primarily affected in about 10 per cent., and becomes involved by extension of suppuration from the right lobe in about 15 per cent. of all cases. The lobus Spigelii is occasionally (3 per cent.), and the quadrate lobe rarely (1 per cent.), the seat of suppuration.

*Number of Abscesses.*—Formerly it was considered to be a characteristic feature of "tropical" abscess of the liver that suppuration was limited to a single cavity; and that, in this respect, these collections of pus offered a marked contrast to pyæmic and other varieties, the usual type of which was supposed to be multiple. Further investigation has failed to confirm this view. *Post-mortem* records show that in Cochin China, Java, and British Malaya, not more than 50 per cent. of amœbic abscesses are single, and personal experience indicates that even this figure is an over-estimate.

MUSGRAVE states that in the Philippine Islands from 40 to 65 per cent. of amœbic abscesses are solitary. Of 562 Egyptian cases examined by ZANCAROL,<sup>6</sup> 60·2 per cent. were single. ROGERS finds that multiple abscesses are frequent in India (32 per cent.), and advances the opinion that they are the result of a mixed infection of staphylococcus and entamœba. Solitary abscesses which are sterile he regards as indicating a purely protozoan origin. FUTCHER, who investigated eighteen instances of amœbic abscess of the liver in the United States, found that only ten were single, whilst in CRAIG'S series of twenty-four cases which originated in the Philippine Islands no more than nine were solitary.

*The size* of amœbic liver abscesses varies greatly. Sometimes

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<sup>6</sup> Zancarol, *Progrès Médicale*, No. 24, p. 393.



they are so minute as to be almost microscopic ; but they are generally large, and occasionally enormous.

*Routes of Infection.*—There are four routes by which *Entamœba histolytica* may reach the liver. They are : (a) Direct, from the lumen of the alimentary canal. (b) Transperitoneal, from the intestinal wall. (c) By the portal vessels. (d) By the general circulation.

(a) From the lumen of the intestine. Unless primary infection of the liver is admitted as a possibility, it is difficult to explain the rare instances of hepatic suppuration in which there has been no precedent dysentery, and the most minute *post-mortem* search has failed to reveal any lesion of the bowel. It is almost inconceivable that intestinal infection should have been so slight as to leave no trace of its presence, and yet to have developed sufficiently to allow penetration of the portal radicles by entamœbæ. It is, however, possible for entry to be effected by the bile-duct. Encysted entamœbæ become active as soon as they reach the alkaline tract of the duodenum ; and, apart from the fact that bile is not secreted continuously, there are many conditions in which it is not necessarily fatal to protozoan life. Living entamœbæ have been repeatedly found in the gall-bladder, where the bile is generally more concentrated than in the ducts.

(b) Direct migration from the diseased intestinal wall into the liver is a frequent method of infection. Superficial amœbic abscesses are often seen on the lower surface of the right lobe, and they can generally be shown to originate in simple extension of the morbid process from the bowel wall. In most of these cases there is ulceration of the hepatic flexure of the colon, and the intestinal walls are thickened, disorganized, and intimately adherent to the lower surface of the right lobe. Even where there are no adhesions the organisms may traverse the peritoneum, by passing

from one serous surface to another. They have often been found in the cavity of the abdomen, and have been specially noted on the capsule of the liver where the gland is uncovered by peritoneum.

(c) In the great majority of instances entamœbæ reach the liver by the portal circulation. When the submucosa is deeply involved they may always be found in large numbers inside the tortuous and dilated venous radicles, and they may occasionally be traced in blood-clots through the whole length of the portal system to their destination in the interlobular veins. The presence of living entamœbæ in portal emboli has already been noted; and there can be no doubt that, whenever amœbic destruction of the intestine is going on, infection is continuous, and as ulceration takes place, enormous swarms of entamœbæ are swept into the portal circulation, and come to rest in the perilobular venules.

No doubt, as has been shown by G. PADOA and others,<sup>7</sup> the protective influence of the healthy liver is sufficient to resist and counteract the entrance of intestinal organisms and their toxins into the systematic circulation, and, in ordinary circumstances, these entamœbæ are all destroyed and absorbed. When, however, the gland is impaired by chronic congestion, infiltration, and fibrosis, it loses its protective function, and the tissues break down around the infecting organism. If, in such cases, the entamœbæ are unattended by septic bacteria, the abscess is solitary and sterile; but, on the other hand, should there be large numbers of putrefactive germs, normal resistance is overcome, and suppuration is then multiple and septic.

(d) Infection of the liver by the systemic circulation. Although rare, infection by this route occasionally takes place. Entamœbæ

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<sup>7</sup> G. Padoa, *Revue Crit. de Méd. Clin.*, September and October, 1904.

are frequently found in the vena cava and in the right heart; and they may undoubtedly reach the tissues by squeezing through the capillaries of the lungs. Amœbic abscesses have been demonstrated in the brain, in the spleen, and in many other situations where direct migration is out of the question.

*Morbid Anatomy and Histology.*—In liver tissue which is about to suppurate, the early morbid changes characteristic of entamœbic infection are generally as follows: One or more minute ash-coloured irregularly spherical nodules develop in the dark-red hepatic structure, and spread excentrically until they are as large as filberts. The general appearance of these patches suggests commencing coagulation necrosis, and, in this respect, they closely resemble certain of the intestinal lesions of amœbic dysentery. The affected areas are bloodless, homogeneous, and solid-looking; when cut, the tissue is glutinous and cheesy; all trace of lobular subdivision is lost; and, if the affected portion is compressed, a few drops of greyish matter ooze out and collect on the surface of the section.

Somewhat later, the adjacent patches unite, and, when about half an inch in diameter, they begin to break down. In some cases, the process is arrested at this stage; and small abscesses, filled with yellowish semi-solid mucus, are often found encysted in the liver. As a rule, however, dissolution and liquefaction take place at the centre of the patch, and an irregular cavity forms which gradually fills with the viscous fluid characteristic of hepatic suppuration.

This matter has little resemblance to ordinary pus. It is usually dull pink or red in colour with a strong "liverish" smell, and a gelatinous consistency which has caused it to be compared, not inaptly, to anchovy sauce. Occasionally, owing to admixture with bile, it is of a greenish colour; and, when contaminated by *Bacillus coli*, it has a distinctly fœcal odour.

As the abscess enlarges by advancing lobular disorganization, the area of coagulation necrosis widens, the contents become more liquid, and portions of necrotic tissue break off from the walls, and float free in the interior of the cavity. These sloughs are generally a notable constituent of the pus contained in "tropical" abscesses ;

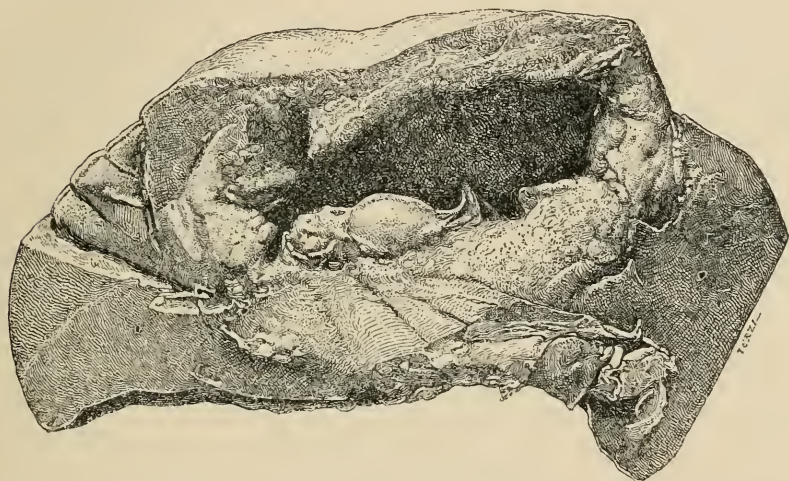


FIG. 28.—Large amœbic abscess of the liver, situated in the right lobe and pointing upwards and backwards. There is no definite wall to the cavity, and the suppurating tissue is surrounded by large areas of coagulation necrosis. (After R. Strong.)

and they indicate extensive and rapid destruction of tissue, with absence of definite limits of suppuration. When they are numerous, there is seldom any pyogenic membrane, and the walls of the cavity are mere projections and fringes of disintegrating hepatic tissue. On the other hand, in the smaller, multiple type of suppuration, the interior of the abscess is generally smooth, and the walls are clearly defined. Occasionally, the vascular structures successfully withstand the lobular destruction ; and strands of blood-vessels and bile-ducts may frequently be seen stretching across the cavity.

When the morbid process is of a malignant type, large areas are involved with extraordinary rapidity, and, in extreme cases, the greater part of the liver tissue may be destroyed almost within a few hours. In these circumstances, encystment or repair is impossible; and it is obvious that unless the destructive process is promptly arrested by the evacuation of the abscess recovery is hopeless.

Under the microscope, the contents of a typical liver abscess are seen to consist of disorganized liver-cells and red blood corpuscles, with quantities of amorphous granular matter, in which fat globules, hæmatoidin, cholesterin, and Charcot-Leyden crystals may sometimes be distinguished. Pus-cells are remarkably few in number, and often altogether absent. Entamœbæ are occasionally found when the abscess is of recent formation; but in cases of some standing they are seldom present in the liquid contents of the cavity. They are, however, generally very numerous in the walls and in the broken-down shreds of necrotic tissue.

Sections of the areas affected by coagulation necrosis show hyaline or granular destruction of the liver-cells, with complete obliteration of their nuclei and outlines. The walls of the interlobular vessels and ducts also become clear and transparent, and all trace of definite glandular structure disappears.

When the type of suppuration is septic and multiple the morbid process is more inflammatory, and the tissues near an abscess are densely infiltrated with leucocytes. Intense reaction may generally be noted round minute foci situated at some distance from the cavity—often actually inside entamœba burrows, which in these circumstances are themselves connected with the interlobular vessels. Sometimes, if a good section is obtained, a small abscess may be seen to have formed inside a branch of the portal vein; and entamœbæ may occasionally be distinguished in the middle of the blood-clot. Softening of the vessel walls, perilobular infiltration,



and formation of a pyogenic membrane by union of the infiltrated foci afterwards take place, and the subsequent course of the morbid process resembles the formation of a pyæmic abscess. Pus-cells and pyogenic bacteria—staphylococcus, streptococcus, and *Bacillus coli*—are found in abundance in the contents of the cavity, and a

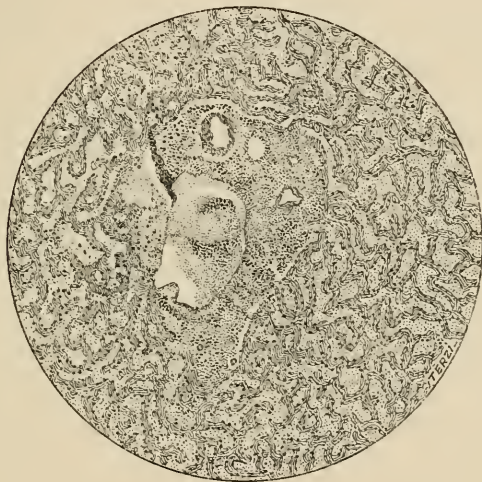


FIG. 29.—The formation of multiple abscesses of the liver as sequelæ of amœbic dysentery. A clot has formed in a small interlobular branch of the portal vein, the walls of which are infiltrated and disorganized. The infection is a mixed one—of staphylococci and entamœbæ, and suppuration has already commenced in the thrombus. The bile-duct and hepatic artery are intact, and their walls practically unaffected. (After Rogers.)

definite pyogenic membrane limits its extent. When the abscess tends to encyst, numerous connective tissue fibres develop in this structure, and it becomes tough, thick and vascular.

*Symptoms, Course, and Modes of Termination.*—In the absence of general hepatitis, the early stages of suppuration may be almost unattended by symptoms; and, in many cases, the first definite



evidence of the formation of an abscess is the pain which is set up by the tension of the fluid in the cavity, and the pressure of the swelling on adjacent structures. Even these indications may be absent; for it frequently happens, especially in the tropics, that a large hepatic abscess passes through its successive stages, matures, and bursts into the lung or the bowel, without serious constitutional disturbance; whilst collections of pus, the formation of which was totally unsuspected during life, are often found after death, encysted in the tissues of the liver.

*Temperature.*—As a rule, however, the symptoms are more distinctive and characteristic, and the thermometer usually affords the earliest and most reliable indications of suppuration. Not infrequently there is a rigor; and the temperature which, after the acute stage of the dysenteric attack, usually remains below normal, rises suddenly to  $103^{\circ}$  or  $104^{\circ}$ . The curve is irregular or intermittent. In most cases it is two or three degrees higher in the evening than in the morning, the daily exacerbations ascending during the development of the abscess by ladder-like increases of  $1^{\circ}$  or  $2^{\circ}$  until they reach a maximum of  $105^{\circ}$ ; whilst each access of temperature lasts but a short time and subsides with copious perspiration within a few hours. The character of the fever is typically hectic and indicative of septic absorption, night sweats being especially severe and persistent.

The periodic increases of temperature are accompanied by headache, thirst, and other constitutional symptoms of fever. Occasionally, but rarely, the thermometer remains continuously high, and the nervous system is then apt to be more seriously affected than when the fever is intermittent. In these cases, most of which have an alcoholic history, headache is intense, and there is generally excitement and delirium. In one patient who was under my own care, the temperature stood at  $104.5^{\circ}$  for over

a week, and acute mania developed on the eighth day. An unsuspected abscess of the liver burst through the lung on the tenth day, with immediate relief of the mental and other symptoms.

*Pain* is also an important clinical feature. It is usually acute and subcostal: and, independently of the position of the abscess, it is generally most intense in the mid-axillary line at the level of the ninth rib. In many cases, however, there is a continuous dull aching over the whole of the hypochondriac region, without localized pain. When the abscess is large and solitary, pain is often referred to the back of the right shoulder, and, not infrequently, to the very tip of the acromion process, a sympathetic phenomenon which is seldom seen in instances of multiple suppuration. To avoid the suffering caused by deep respiration, and by the weight of the liver dragging on its inflamed attachments, the patient lies on the back or the right side, and the breathing is shallow and thoracic.

If there is perihepatic inflammation, tenderness on pressure is a prominent symptom. Although usually most marked at the margin of the costal arch in the mammary line, it is sometimes widely distributed; and palpation between the ribs causes intense pain all over the liver area. Perihepatitis almost invariably originates in infiltration and infection of the enveloping membranes of the liver by pus; it is, in consequence, frequent when suppuration is multiple and septic, and it is seldom seen when the abscess is sterile and solitary. Further, as it is generally set up by the approach of the abscess to the surface of the liver, it is usually a late symptom; and when the cavity is deeply situated or encysted, tenderness and perihepatitis are often altogether absent.

*Physical Signs.*—Alterations in the size and shape of the liver naturally depend on the extent and position of the abscess, but in most cases enlargement is a prominent physical sign. There is generally considerable bulging of the right side, the intercostal

spaces are unduly prominent, and the angle of the cartilages with the middle line is widened. When an abscess forms near the upper surface, the dome of the right lobe pushes the base of the lung up into the thoracic cavity; and in the prone position the upper limit of dulness is considerably higher than normal. A line drawn from the lower angle of the scapula to the fifth interspace in the axillary line commonly marks the extent of the alteration in the size of the liver, whilst fine *râles* and crepitation indicate the effects of pressure on the lung tissue.

When the seat of suppuration is near the inferior aspect, the liver enlarges downward; and the lower border generally extends one or two inches below the costal cartilages. In thin patients, when there is great enlargement, the abscess may occasionally be directly palpated through the abdominal walls; and it is then felt as a soft tumour in the middle of a smooth brawny mass which reaches, in some cases, to the umbilicus. If the cavity is superficial and low down, fluctuation may sometimes be elicited below the costal margins; but under the ribs it is disguised by the elasticity of the intercostal tissues and is apt to be very deceptive.

The later symptoms indicate general septicæmia.

*The facies* is characteristic, often almost pathognomonic. The expression is one of intense weariness, and the complexion is sallow or mud-coloured; the conjunctivæ are yellowish, or greenish yellow, but jaundice, even although large tracts of the liver are involved, is infrequent unless there is direct compression of the main bile-duct. The skin is lax and flabby; emaciation and muscular wasting are rapid and severe; and there is usually great exhaustion and sleeplessness. The dysenteric symptoms are seldom influenced by the development of an abscess; but in cases of a marked septicæmic character, severe and even fatal attacks of choleric diarrhœa are not unusual.

*The urine* is characteristic of the general condition, and unless there is marked septicæmia and high fever it seldom contains albumin. Urates, chlorides and urobilin are in excess; whilst, owing to the destruction of liver tissue, the excretion of urea is generally diminished.

*The blood.*—In many instances, there is a polymorphonuclear leucocytosis which increases with the progress of the disease; but this symptom is extremely inconstant, and no reliance can be placed on differential blood-counts as an indication of the formation of pus. The total number of leucocytes is usually high, and varies from 15,000 to 20,000.

*Modes of Termination.*—The terminal signs and symptoms depend on the direction in which suppuration extends. Occasionally, but rarely, the abscess pushes its way towards the surface, and the skin and tissues become inflamed and œdematous over the most prominent part of the swelling. Much more frequently—in about 60 per cent. of all untreated cases—it points upwards, and the symptoms are then chiefly respiratory. There is a marked diminution of the breath sounds; and there are physical signs, first of pleurisy, then of localized empyema, and finally of destructive compression of the lung. The sequence of events is usually very rapid. Cough becomes persistent and almost continuous, whilst at intervals there are attacks of dyspnœa of an aggravated choking character.

Ultimately, to the marked relief of the patient, the abscess bursts during a fit of coughing, and an enormous quantity of matter, or anchovy-sauce sputa, containing numbers of entamœbæ, blood-corpuscles, and hæmatoidin crystals, is expectorated through the air-passages. When free communication is established with a bronchial tube, the extravasation of pus into the lung is arrested by adhesive inflammation, and the contents of huge abscesses of the liver are often evacuated rapidly and safely by this route. On the

other hand, when the course of the disease is more chronic, and especially when the surrounding alveoli become extensively infiltrated with pus, the termination is apt to be less favourable.

Rupture into the peritoneal cavity is, unfortunately, very common, not less than one out of every five cases tending to terminate in this way. When the abscess is a large one, a fatal result is almost inevitable, even although laparotomy is performed at once; but when it is small and sterile, recovery is not unusual. Fatal peritonitis is, obviously, more liable to be set up when the contents of the cavity are septic; but even in such cases leakage from a small abscess may take place without serious result. Probably this occurs more frequently than is generally supposed; for collections of calcified pus, in association with old cicatrices in the liver, are often found in the peritoneal cavity at *post mortem* examinations; and after hepatic attacks patients not infrequently complain for many months of localized abdominal pain and tenderness.

Approximately, ten per cent. of all untreated abscesses burst into the colon, and one per cent. into the small intestine. Adhesions form readily, and are generally very abundant round the folds of the bowel and omentum; and when rupture takes place in this situation the percentage of recoveries is fairly high. When pus is evacuated into the colon, it is passed almost immediately by the rectum; and, being unaltered in appearance, it is readily recognized; but when it comes from the small intestine it is often so much changed that it is mistaken for an ordinary dysenteric stool, and the change in the condition of the patient may be overlooked.

The bursting of a hepatic abscess into the stomach is infrequent, although, on account of its fatality, this termination is surgically of great importance. Actual rupture generally occurs during a fit of vomiting, but it is preceded by urgent symptoms of pressure and irritation; and when acute gastric pain, with intense nausea and



sickness, supervenes during the development of an abscess, operative interference is always indicated. Probably because suppuration in these cases is often limited to the left lobe, the results of opening an abscess which is pressing on the stomach are by no means unfavourable, but unless free drainage to the outside is established at an early period practically every case proves fatal. Death is generally due to adhesions being torn asunder by the violence of the gastric movements, and consequent escape of fluid into the abdominal cavity.

Several cases are on record in which liver abscesses burst into the pericardium, or into one of the venæ cavæ, death being, of course, instantaneous. Rupture into the pelvis of the right kidney, with subsequent discharge of hepatic pus by the urethra, and ultimate recovery, has also been reported.

It must not be forgotten that the contents of an amoebic abscess are not always evacuated, and that apart from the relative frequency of these terminations, a considerable number of cases end in encystment. In such instances, the symptoms are seldom very characteristic; and it is impossible to form even an approximate estimate of the proportion of liver abscesses which terminate in this way. Probably, however, in not less than twenty or thirty per cent. of all cases in which pus has actually formed, the suppurative process gradually diminishes in intensity, and the abscess becomes encapsuled in the liver tissue.

*Diagnosis.*—A seizure of malarial fever occurring soon after an attack of dysentery is the condition most likely to be confused with abscess of the liver, and if hepatitis is superadded, differentiation may be very difficult. In former years the aspirator was freely used in all cases in which there was the slightest doubt, and the instrument came to be regarded as a routine method of diagnosis; but it is now considered unjustifiable to resort to exploratory puncture



unless the suspicion of suppuration is definitely confirmed by other symptoms. In all tropical cases, preliminary exclusion of malaria is essential ; for although a positive result in a search for malarial parasites does not preclude the possibility of abscess, it should indicate caution in advising operative interference.

Empyema, suppuration of the gall-bladder, pyelephlebitis, and subphrenic abscess are conditions which must also be borne in mind as possible sources of error ; but hydatids and other tumours are unlikely to be mistaken for acute suppuration. It may, however, be difficult to distinguish them from quiescent or encysting abscesses.

*Prognosis.*—The prognosis is always grave, and although the mortality has been greatly reduced by early treatment and prompt surgical intervention, from 30 to 40 per cent. of all cases of post-dysenteric abscess of the liver still prove fatal. Recuperative power is, however, remarkable, and the extent to which hepatic tissue may be destroyed and repair yet take place is almost incredible. In a case which came under personal observation, an abscess developed in the right lobe of the liver of a male adult of good constitution during a mild attack of dysentery. Arrangements were at once made to evacuate the pus, but about an hour before the time fixed for operation the patient was seized with a violent attack of coughing, and brought up over two pints of “anchovy” sputum, with subsequent relief of all the symptoms. A week later, a tumour formed below the costal margin, and preparations were again made to operate, when a large quantity of hepatic pus was unexpectedly discharged into the great intestine. Once more convalescence seemed to be at hand, but a fortnight afterwards an abscess pointed at the ninth interspace in the mid-axillary line. The cavity was opened and drained, and the patient ultimately made a complete recovery.

## CHAPTER XVI.

## OTHER SEQUELÆ OF AMŒBIC DYSENTERY.

METASTATIC abscesses are not confined to the liver, and true amœbic suppuration occasionally occurs in viscera far removed from the areas of original infection. The brain is, perhaps, most frequently affected: but numerous instances are recorded of amœbic abscesses in the spleen, the salivary glands, the alveolar and buccal tissues, the psoas muscles, the perirenal sheaths, and the kidneys. Moreover, although the rectum itself is seldom affected by amœbic disease, most of the large ischio-rectal abscesses which are so common in the tropics originate in penetration of the intestinal wall by the specific organism of dysentery.

CEREBRAL ABSCESS.—In countries where amœbiasis is endemic, abscess of the brain is unusually prevalent, and the frequent association of the condition with a history of dysentery indicates that the pathological connection may be closer than is generally suspected. In Egypt, Kartulis found <sup>1</sup> secondary cerebral suppuration in 3 per cent. of a series of cases of amœbic abscess of the liver; and recent investigations show that it is equally frequent in Java and the East Indies.

The abscesses are usually very small—in many cases they are microscopic—and they are generally situated near the surface of the cerebrum in close proximity to a large sinus or lymph channel.

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<sup>1</sup> Kartulis, *Central. f. Bakt.*, Bd. 37. 1904.

The appearance of the cavities is characteristic. In contradistinction to the greenish-tinted and extremely offensive pus found in cerebral abscesses which are a result of cranial disease, the contents of amœbic abscesses of the brain are generally odourless, and of a deep yellowish or brownish-red colour. There is also, in most cases, a true pyogenic membrane ; and sections through the abscess



FIG. 30.—Amœbic suppuration of the brain. Section of a minute abscess. The cavity contains numerous entamoebæ and pus corpuscles. The nuclei of both are deeply stained. (After Legrand and Dopfer.)  $\times 300$ .

reveal the presence of large numbers of entamoebæ floating free in the pus or embedded in the walls and surrounding tissues. LEGRAND states<sup>2</sup> that amœbic abscesses of the brain are seldom sterile, and that besides entamoebæ various bacteria, both aerobic and anaerobic, may be recovered from the interior.

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<sup>2</sup> Legrand, *Deutsch. med. Woch.*, p. 1905.

Abscess of the brain, as a sequela of dysentery, has long been familiar to physicians, and the following notes of a case which was treated by Habershon in Guy's Hospital over fifty years ago, supply an interesting clinical and *post mortem* record of metastatic cerebral suppuration, and are, indeed, a typical example of a fairly common tropical condition.

*Chronic Dysentery. Hepatic Abscess. Pyæmia. Abscess in the Brain and Lung.*—Thomas D., aged 25, was admitted February 14, and died March 19, 1855. He was a sailor, and had been for two years in the East Indies. In Burmah he had ague and dysentery, and was ill for several weeks; and for two months he had had pain in the side.

On admission, he was sallow and generally cachectic. There was pain in the right side; the chest was dull; and it was supposed from the history that he had abscess in the liver.

On February 21, when sitting by the fire, he fell down in a fit, and was convulsed; for several days he continued in a semi-conscious condition. On the 28th, he could speak and give his name; he continued apparently to improve till the 14th, when he again fell into a semi-conscious state. On the 16th he was able to sit up and take his breakfast, but shortly afterwards he became quite insensible, and had stertorous breathing which continued till death. It was observed throughout that the right leg was weak, and that at last it was paralysed. The right pupil was smaller than the left, but a few hours before death it became widely dilated.

On inspection twenty-four hours after death the outside of the brain was dry, and at the base there were slight adhesions between the surfaces of the arachnoid. In the posterior lobe of the left hemisphere there was an abscess about the size of a hen's egg, containing thick, tenacious pus, which nearly reached the surface, and was surrounded with softened brain substance; at its anterior part there was a clot of blood, also surrounded by softened tissue. The abscess had broken into the posterior corner of the left lateral ventricle, which was filled with pus; the right contained about an ounce of clear serum, and the fourth ventricle was healthy.

In the chest old and recent adhesions were found at the bases of

both pleural cavities. The bronchi were slightly inflamed, and contained muco-purulent secretion. The base of the left lung contained a small abscess, the base of the right was in a state of incipient pneumonia.

In the right lobe of the liver at the upper surface there were two chronic abscesses, containing about three ounces of pus; it was viscid and green, and the walls of the abscess, which were very thick, were bounded by a smooth cyst and firm tissue about one eighth of an inch in thickness; on the circumference of the abscess a compressed vein was observed.

In the colon the mucous membrane was thickened; several well-marked cicatrices were found in the ascending colon; the mucous membrane was puckered; and in some parts it was of a slate colour, the muscular coat being slightly hypertrophied.

Unless located and opened at an early stage, cerebral abscesses are almost inevitably fatal, although in some instances, if the suppurating area is limited in extent, encystment may take place. When the amœbic cavities are numerous and small they tend to coalesce and to form worm-eaten channels on the surface of the brain; but suppurative meningitis appears to be very uncommon.

**ABSCCESS OF THE SPLEEN.**—Suppuration of the spleen is generally regarded as a rare complication, but several instances have lately been described in which splenic abscesses developed as a result of amœbic infection, and many typical specimens of the condition are to be found in museums of tropical pathology. In a recent case reported to the Society of Tropical Medicine and Hygiene by PRESTON MAXWELL,<sup>3</sup> of Amoy, an abscess of exceptional size developed in the spleen of a young Chinaman a month after the first symptoms of dysentery. The swelling completely filled the left half of the epigastrium and projected over to the right of the mesial line; there were daily rigors which simulated a double infection of benign tertian<sup>m</sup>, malaria, and, in the dejecta, which were

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<sup>3</sup> Society of Tropical Medicine and Hygiene, *Transactions*, July, 1909.



dysenteric in character, *Entamœba histolytica* was found. The spleen was incised through the abdominal wall, and 80 oz. of yellow pus and blood were evacuated, the patient making a good recovery. Large numbers of entamœbæ were present in the contents of the abscess cavity. The liver was healthy.

When suppuration takes place in the spleen it is generally extensive, and, in the great majority of instances, is fatal. The route of infection is uncertain: in a few of the cases which have been reported the organisms appeared to invade the viscus directly from the splenic flexure of the colon, but the blood-stream is probably the usual channel.

AMŒBIC APPENDICITIS.—The appendix is obviously liable to be involved in the organic lesions of all varieties of dysentery, although, except as part of the general morbid process, amœbic appendicitis is rare. That metastatic appendicitis, strictly so called, occasionally originates in amœbic infection, and that peri-appendicular suppuration may be secondary to insignificant amœbic lesions in the colon there can, however, be no doubt. *Entamœba histolytica* has frequently been demonstrated in the walls of excised appendices and in pus from the region of the cæcum, although there has been no history of dysentery and nothing to indicate amœbic infection. On the other hand, the results of careful searches for entamœbæ in a large number of consecutive cases of appendicitis have been negative.<sup>4</sup> Differentiation between amœbic and non-amœbic disease of the appendix is generally impossible, and as the treatment is practically the same it is unimportant. Early surgical intervention is advisable in every instance in which a definite diagnosis of appendicitis has been made.

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<sup>4</sup> See papers by Leo Schredel (*Wiener. klin. Rundschau*, March 14, 21, 28, 1909) ; also, Report by Sozo Nishiyama (*idem*).



INTESTINAL HÆMORRHAGE.—Dangerous bleeding from the intestine, although rare, is occasionally encountered in the course of amœbic dysentery; and HAASLER,<sup>5</sup> and STRONG<sup>6</sup> have shown that this grave complication is especially liable to occur during the formation of a hepatic abscess. The frequent combination of the two conditions is now fully confirmed, and numerous instances of their association have been reported by FUTCHER, MUGLISTON, FREER,<sup>7</sup> and other observers. The nature of the relationship is somewhat obscure, but STRONG has recently pointed out that in the cases in which it was noted there was a marked diminution in the coagulability of the blood. Fever was also a prominent and persistent symptom, and jaundice occurred more frequently than in simple abscess of the liver. The evidence indicates that predisposition is an important factor, and that the condition is probably one of failure of resistance to septic infection.

In view of the great destruction of the vascular coats of the intestine, severe bleeding might have been expected to be a more general symptom of amœbic dysentery than is actually the case. Alarming hæmorrhage from amœbic ulcers, for instance, is less frequent than it is from the smaller necroses of typhoid fever, or of duodenal ulcer; and the explanation of this comparative immunity is by no means clear. It is true that the type of disease is more chronic, and that endarteritis, infiltration, and thrombosis usually precede tissue destruction; but in many instances of amœbic dysentery ulceration is both rapid and extensive, although only an insignificant amount of blood is passed in the dejecta. As has been seen, the blood-vessels often show a remarkable resistance to ulcerative processes.

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<sup>5</sup> Haasler, *Deutsche. med. Wochen.*, 1902.

<sup>6</sup> Strong, Publications of the Biological Laboratory, Manila, 1905.

<sup>7</sup> Mugliston and Freer, *Journ. Trop. Med.*, 1905.

GASTRO-INTESTINAL COMPLICATIONS.—Except in cases of profoundly impaired nutrition, the mouth is seldom affected in amœbic dysentery; but, in the poorest class of patients, *cancrum oris* is a somewhat frequent complication. Malignant stomatitis is, however, more commonly seen as a concomitant of the bacterial form of the disease and of the dysentery which, in the tropics, so frequently precedes the fatal issue of tuberculosis, nephritis, diabetes and other chronic dyscrasias. It can, therefore, scarcely be regarded as a complication, for the association is with general malnutrition rather than with specific infection.

Non-malignant stomatitis is very rare. The distinctive eroded ulcers of sprue have no relation to amœbic dysentery, and are found only when the disorder of which they are symptomatic has become established.

Gastralgia, gastric catarrh, and dyspepsia are often described as late complications of amœbic dysentery; but although some degree of digestive incompetence generally persists after the active symptoms have subsided, affections of the stomach rarely appear as true sequelæ of the disease.

In most cases, dyspeptic troubles are undoubtedly the result of remedial measures. Pain, nausea and vomiting are frequently induced by persistent attempts to irrigate the lower bowel; and, when there is a tendency to gastric derangement, these symptoms are always increased by the use of copious injections. That various forms of neurosis originate in this way, there can be no question; and absorption of toxin is especially liable to take place in young subjects. In a recent instance, two children who were being treated for chronic amœbic dysentery were severely affected, and rectal irrigation had to be abandoned, as it was invariably followed by violent sickness, and on one occasion by tetany.

Gastric ulcer is very rare, but hyperchlorhydria and subacidity

are often remarked during convalescence, and in the quiescent stages of dysentery. So frequent are those symptoms, indeed, that it is almost reasonable to assume a definite connection between them and amœbic infection.

The condition which is described as chronic amœbic enteritis is, in the great majority of cases, sprue. Except by direct extension upwards, the small intestine is seldom affected in amœbic dysentery, and permanent lesions or sequelæ are certainly very rare. An affection of the upper bowel consequent on amœbiasis is said to be prevalent in Cochin China and in other parts of the Eastern tropics, but when a patient is carefully examined, mouth sores, contraction of the liver, and other distinctive signs of sprue are generally found.

The morbid changes of the great intestine which result from amœbic dysentery have already been described. Together with the concurrently-formed peritoneal adhesions, these structural alterations of the colon give rise to permanent pain and tenderness, and are of so constant a character that they may fairly be included among the distinctive sequelæ of the disease. The pain is generally persistent rather than severe, and it is aggravated by movement, by the erect attitude, by a full meal, or by any cause of intestinal distension. It ceases on the patient lying down; but tenderness, although insignificant when standing, is generally increased in the recumbent position. If accidental diarrhœa comes on, or if a purgative is taken, the pain is altogether disproportionate to the intestinal disturbance; but purgation is usually followed by a corresponding measure of relief.

The condition is always chronic, and it is often combined with manifestations of persistent intestinal auto-intoxication. In such cases, the countenance is sallow or muddy; and there is generally great vital depression with marked secondary anæmia and emaciation. Not infrequently, also, there are evidences of splanchnoptosis

and other visceral neuroses, the symptoms then chiefly affecting the nervous system. At this stage, neurasthenia, loss of mental tone, and melancholia are not unusual.

NERVOUS DISEASES.—Apart from mental impairment, it is now generally admitted that various derangements of the nervous system may originate in amœbic disease; and the interdependence of gastro-intestinal and nervous function on which neurologists lay so much stress is, perhaps, nowhere better illustrated than in the circumstance that disorders like chorea and epilepsy have, in many instances, been definitely traced to attacks of amœbic dysentery. Peripheral neuritis is also an occasional sequela, especially after middle age; but the connection is often difficult to establish, as in countries where amœbic dysentery is endemic other causes are generally responsible for the condition.

Chorea is a frequent consequence in young subjects; and inco-ordination and spasm are extremely liable to be induced by an attack of dysentery if the patient suffered during early youth from these forms of nervous weakness. MUSGRAVE has published<sup>\*</sup> two cases which indicate the close association of the disorders. In one of them an attack and a relapse of amœbic dysentery were followed in each instance by chorea, although, after typhoid fever, the patient had no nervous symptoms.

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<sup>\*</sup> Musgrave, "Amœbiasis: Complications and After Effects," *Philippine Journ. of Science*, June, 1906.



PART VII.—TREATMENT.





## CHAPTER XVII.

## THE PROPHYLAXIS OF AMŒBIC DYSENTERY.

IT has been shown that every case of amœbic dysentery originates in the ingestion of the pathogenic entamœba, and that, unless there is contamination of water or food by the dejecta of infected persons there can be no occurrence of the disease. It follows, therefore, that the first step in prevention is the destruction or efficient disinfection of the excreta of patients who are suffering from dysentery. Further, as it is apparent that infection, in the great majority of instances, is waterborne, the most effective measure of general prophylaxis must be to secure a public water-supply which is absolutely beyond suspicion.

In several of the more important cities and settlements of the tropics the installation of a pure water supply has been satisfactorily accomplished, and, in practically every instance, the effect on the public health has been immediate and striking. In these places, amœbic dysentery has lost its endemic character, and, although by no means wholly eradicated, the disorder now occurs only in sporadic form, and as a consequence of infection by vegetables, fruit, and other less important agencies. On the other hand, most of the great tropical centres of population are still without reliable drinking water ; and, in many cases, the public provision of a plentiful supply of pure water appears to be almost impossible. The difficulties are mainly geographical, and are

chiefly felt in districts where there are no hills, and where a river furnishes the only available source of supply; for although, in ordinary circumstances, water may be effectively purified during a comparatively short flow in a stream, river valleys in the tropics are generally so densely populated that freedom from pollution is unattainable.

Even when a town supply is collected from an uninhabited jungle catchment area, and is stored in an impounding reservoir, adequate supervision is extremely difficult; and it is always advisable, in districts where amoebic dysentery is or has been endemic, to take further precautions. Almost everywhere in the tropics sterilization of the domestic supply is necessary; and it is a sound principle to make it an invariable rule to *boil all drinking water*; and, after boiling, to keep it as far as possible sterile.

Enough has been said about the growth of amoebic organisms on filters to show that, unless carefully looked after, these appliances may constitute a source of serious danger. When there is much sediment in water, a filter should be employed as a preliminary measure; but filtration in itself is useless for sterilization, and may, indeed, prove a source of fresh contamination. As a rule, filters are unnecessary; and on no account should drinking water be filtered *after* it has been boiled.

With reference to milk, although its freshness and nutritive value are to some extent impaired by boiling, the risks of pollution are again so great and so insuperable that cow's milk should also be sterilized in the same way. The utility of Pasteurization, or the employment of lower temperatures than 212° F., is doubtful. Entamoeba cysts are highly resistant to heat, and experiments show that they are capable of surviving a temperature which will kill most varieties of encysted bacteria.

Special precautions should also be employed with regard to

certain articles of common consumption. Lettucés, radishes, tomatoes and salads, unless grown under reliable supervision, are dangerous, and should be rigorously excluded from the household dietary. Even when sanitary cultivation is assured, uncooked vegetables are always suspect; for nothing is more difficult than to convince a native gardener that vegetables will grow without plentiful supplies of liquid manure, and nothing is harder than to dissuade him from its use.

Cold meat, fish, chicken, &c., must be carefully protected from contamination. Many families in the tropics make it a rule to have no meat on the table unless it has been brought direct from the fire; but this stringent regulation excludes a large number of desirable and economical dishes, and if meat safes and wire-gauze covers are kept scrupulously clean and are judiciously used for the storage of cold meat, bread and similar things, they afford sufficient protection. Cold meat should never be garnished with raw vegetables or green herbs.

In most tropical cities, the manufacture of aerated waters is now an industry of considerable importance, and soda water, lemonade and other beverages of the sort are largely utilized as table waters. In most cases, they are quite safe; but their source should always be known, and if there is any suspicion of insanitary manufacture or of misrepresentation as to their origin they should be carefully avoided. The same caution applies to ice; unless made from absolutely pure water, it may be highly dangerous, and there is no doubt that sherbet and other drinks displayed on booths in native bazaars are frequent sources of infection.

Apart from special methods of prevention, resistance to the invasion of entamœbæ depends, to a great extent, on adequate digestion and unimpairment of the general health. When vitality is lowered by exposure, improper food, and fatigue, infection is easy

and frequent ; when the normal tone of the system is maintained by regular habits, suitable diet, and adequate exercise, infection is difficult and rare. It is always necessary to guard against chills, which in the tropics are among the most frequent causes of intestinal catarrh. After exercise, a dry jersey, or sweater, should be put on and moist underclothes should be changed as soon as possible. In places where there is a marked fall in the atmospheric temperature during the night, a woollen abdominal belt should be worn ; and, generally speaking, exposure to damp and cold should, as far as possible, be avoided.

In the tropics, as elsewhere, measures designed for the prevention of intestinal disease must be systematic and continuous ; and it is essential that they should conform as far as possible to the arrangements and comforts of everyday life. If prophylaxis ceases to be reasonably pleasant as well as practicable it will not be carried out. The continued use of distilled or boiled water at meals is always distasteful, and frequent change is necessary. Barley water, China tea (with fresh limejuice instead of milk), and aerated waters, with some variety of fruit extract, provide an agreeable and welcome change.

The alcoholic drinks which are least likely to predispose to intestinal catarrh and consequent liability to specific infections are weak dilutions of spirits or some variety of white wine in soda-water. Hock, Moselle, Sauterne, Graves, and Chablis of good quality can generally be easily obtained, and these wines are more suitable for hot climates than claret and burgundy. In British tropical settlements whisky or brandy and soda is in general use as a table beverage ; and if well matured, freely diluted with good aerated water, and taken in moderation, it is fairly innocuous. Liqueurs, bitters, and concentrated wines, such as sherry, port, and Madeira, should be avoided.

There is no foundation for the assertion that the free use of alcohol tends to produce immunity; the chronic gastritis inseparable from alcoholism actually predisposes to infection; and the statement is, moreover, entirely contrary to clinical experience. As a matter of fact, alcoholic subjects are especially liable to amœbic dysentery.

The beneficial influence which may be exercised by keeping men in good physical condition, by looking after their general hygiene without fuss or unnecessary irritation, and by carrying out reasonable precautions with regard to their food and drinks, is well exemplified by the decrease in the case incidence of amœbic dysentery among the American troops in the Philippine Islands since special sanitary regulations for the prevention of the disease were introduced. As compared with white civilians resident there, of whom from 15 to 20 per cent. are annually affected by amœbic dysentery, not more than 3 per cent. of the soldiers of the army of occupation are now treated for the disorder in the garrison hospitals.

The general prophylaxis of amœbic dysentery may almost be summed up in one word—cleanliness. If domestic arrangements are closely supervised, if a plentiful supply of hot water is provided in the kitchen, if plates and dishes are scalded when washed, and afterwards dried with clean cloths, if water and milk are boiled, if food is kept from contamination by flies and other carriers of pollution, if larders and meat safes are systematically cleansed—in short, if the sanitary routine of a well-arranged house is made compulsory, there is little danger of contracting amœbic dysentery, even in places where endemic infection is intense and persistent.



## CHAPTER XVIII.

## THE TREATMENT OF ACUTE AMŒBIC DYSENTERY.

IT has been seen that in a considerable proportion of cases of amœbic dysentery the periods of onset and relapse are attended by clinical manifestations of marked severity, and that the disorder is then liable to assume a grave and malignant aspect. It follows that during these attacks prompt attention and careful management are of special importance, not only in relieving the urgency of the symptoms, but in averting the occurrence of dangerous complications.

At this stage, however, active specific treatment is seldom practicable, and remedial measures are chiefly designed to mitigate the severity of the seizure and to tide the patient over an illness, which, although only an incident in the course of a chronic infection, may at any time induce a crisis of imminent danger. The general indications are to relieve pain, to keep fever in control, and to check the incessant attempts at defæcation; and in order to effect these objects, absolute rest in bed and efficient and capable nursing are essential. During the exacerbations of amœbic dysentery it is specially important that all unnecessary movement should be avoided and that the systematic use of a bedpan should be made imperative.

When there is much pain and tenesmus, treatment ought to commence with the hypodermic injection of  $\frac{1}{3}$  gr. of morphia, and a careful abdominal and rectal examination should then be

made. If scybala are present, or if, as is generally the case, there is evidence of irritation from retained faecal matter, a large intestinal douche (2 to 3 pints) of warm (98° F.) solution of boracic acid ( $2\frac{1}{2}$  gr. to the ounce) should be administered. If necessary, this may be repeated; and after the colon and lower bowel have been emptied in this way, a small enema of starch, mucilage of acacia, or some other demulcent, generally affords effective relief to the rectal spasm and irritability. It is inadvisable to inject anodynes, such as laudanum and cocaine, into the rectum, as in acute dysentery absorption is extremely irregular and uncertain, and serious symptoms are not infrequently produced by apparently small doses. If the stomach contains undigested food, an emetic of mustard and hot water should be given at once.

In most cases, the purging and distress consequent on continuous efforts at evacuation are immediately relieved by the morphia; but, if the hypodermic injection is not repeated within a few hours, the tenesmus and other symptoms usually recur with undiminished violence. Unless the pain is excessive, it is, however, inadvisable to push the morphia farther; and, at this stage, the best effect may generally be obtained by giving a cachet containing  $2\frac{1}{2}$  gr. of calomel with  $\frac{3}{4}$  gr. of pulv. opii. This combination should be repeated every two hours until four doses have been taken.

An old, although latterly somewhat discredited remedy, calomel is often of very great service in acute amœbic dysentery; and, unless there are cogent reasons which forbid the use of mercury, no hesitation need be felt in ordering it. The principal indications against the employment of the drug are idiosyncrasy—which is especially frequent in persons of East Indian birth—marked anæmia or prostration, stomatitis, and œsophagitis. The huge doses (20 or 30 gr.) in which calomel was formerly prescribed are responsible for the disrepute into which it has fallen, for although there is

abundant testimony that, in the hands of ANNESLEY, MOREHEAD, and many of the older physicians, excellent results were often obtained by the use of the drug, it is not surprising, in view of the enormous quantities which they gave, that its administration was occasionally followed by collapse. There does not, however, seem to be any ground for the belief expressed by HABERSHON and WILKS (who opposed the employment of mercury in all intestinal diseases), that in dysentery calomel always increases the inflammation of the mucosa. On the contrary, in moderate doses, it undoubtedly acts promptly and satisfactorily by hastening the removal of retained matter, by stimulating the biliary and intestinal secretions, and, possibly, by the exercise of its powerful antiseptic and germicide properties.

When calomel cannot be taken, small and frequently repeated doses of sulphate of magnesia or sulphate of soda generally prove an efficient substitute. A concentrated solution—1 drachm in an ounce of aq. chloroformi or aq. cinnamoni—should be given every two hours, until an ounce of the salt has been taken. The best effect is obtained if water and fluid nourishment are withheld for half an hour before and half an hour after the administration of the medicine. Opium should never be combined with saline remedies ; but, if necessary, morphia may be used hypodermically.

In the earliest stage food must be reduced to a minimum, and for the first twenty-four hours the diet should be restricted to albumin water (the whites of two raw eggs to 10 oz. of water), whey, barley water, toast water, or weak milk and soda (milk 1, soda 3). Solids must not be given, nor should any food, such as undiluted milk, which is likely to form a bulky residue in the colon, be allowed. During the exacerbations of amœbic dysentery in the tropics, thirst is always intense ; it may be relieved by small quantities of ice, or iced water ; and cold tea, with fresh limejuice instead of milk and sugar, often proves an effective remedy.

At the end of twenty-four hours, if the symptoms show some abatement, a large cupful of strong chicken broth or meat juice may be given, and if the improvement is maintained, soups, eggs, and fluid meat, may be tried and should form, practically, the sole food until the end of the attack. Minced chicken, fish, sweetbread, &c., may usually be given about the fourth day. Farinaceous foods and undiluted milk generally disagree with patients in the acute stages of amœbic dysentery.

When pain is an urgent symptom, hot fomentations should be applied to the abdomen. The most effective method of preparing a fomentation is to fold a length of flannel in eight or twelve layers, and after soaking in boiling water to wring it out in a twisted towel. Before application a few drachms of linimentum opii or turpentine are sprinkled on to the surface, and the flannel is then packed, as hot as the patient can bear it, firmly on to the abdomen, where it is allowed to remain until it begins to cool. When properly prepared and carefully applied at short intervals, the amelioration of all the symptoms of acute amœbic dysentery—and notably of the tenesmus and straining—which follows the application of these stupes is often very remarkable, and should a relapse occur they are generally the first remedy to be asked for.

During acute attacks the temperature must be carefully watched, and if a tendency to hyperpyrexia is observed, a concomitant infection of malaria should be suspected. If parasites are found in the blood, and especially if the small ring forms of malignant tertian are discovered, an intramuscular injection of quinine should be given at once. For this purpose, 15 grains of bi-hydrochloride of quinine are dissolved by heating in a test-tube with 100 minims of distilled water, the whole of the solution being then injected into the gluteus maximus muscle. It is unnecessary to add that on every occasion on which injections are used, the syringe and needle

should be sterilized, and the skin carefully cleansed and disinfected. In such cases administration of quinine by the mouth is inadvisable; for, apart from the fact that vomiting is generally an urgent symptom, absorption is always defective, and the action of the remedy may be delayed until it is too late. Cold packs are generally necessary in malarial, and are always indicated in non-malarial hyperpyrexia.

Fever is almost invariable during exacerbations of amœbic dysentery, but a moderate degree of pyrexia ( $102^{\circ}$  to  $104^{\circ}$  F.) seldom calls for active treatment, and the temperature generally subsides with the administration of calomel and free action of the bowels. Frequent sponging with tepid water—part only of the body being uncovered at a time, and other precautions being taken against chill—is often effective in reducing the temperature and in promoting the general comfort of the patient. Warm sponging is, moreover, generally successful in soothing the nervous system, in controlling excitement, and in inducing sleep. If the fever does not yield to these simple measures, acetanilide (in  $2\frac{1}{2}$ -grain doses) may be tried. When moderate pyrexia is accompanied by severe headache, with high vascular tension—a frequent condition in acute dysentery—antipyrin is the best remedy.

Stimulants are rarely necessary, and in ordinary cases are harmful; but if collapse threatens, brandy should be given freely. The best effect is generally obtained by a moderately small dose—a tablespoonful in half a tumblerful of very hot water—repeated three or four times at intervals of half an hour. If there is much sickness stimulants may be administered by the rectum, but subcutaneous injection of normal saline is preferable (see p. 212). As intense prostration often supervenes unexpectedly and is a frequent cause of death during acute exacerbations, stimulants and normal saline should always be available, although there may appear to be no immediate necessity for their use.

Mental complications are rare, but they occasionally develop during an acute attack of amœbic dysentery, and naturally occasion much anxiety. Delirious excitement is one of the most usual forms of derangement, and it is generally connected with a previous malarial infection. When pyrexial delirium appears to be imminent, a hypodermic injection of quinine (10 grains) to which 2 minims of solution of hyoscine (1 grain to 200 minims) have been added, must be given at once. If the temperature falls without relief to the mental excitement, the hyoscine may be cautiously repeated until the patient falls into a deep sleep. When hyoscine is unavailable, morphia is preferable to other sedatives. In the only instance in which I have seen bromides prescribed, they appeared to exercise an unusually depressant and unfavourable influence ; for exhaustion set in almost at once, and the case terminated fatally within a few hours.

Vomiting is seldom a prominent symptom unless there is high fever ; but in some instances it is persistent, and it always demands special attention. Counter-irritation is generally the best remedy ; mustard or strong turpentine stupes should be applied to the stomach, while the patient is kept lying down and is supplied with small pieces of ice to suck. When anything can be retained, tablets of cocaine,  $\frac{1}{20}$  of a grain (repeated every quarter of an hour until five have been taken), relieve the intense nausea more effectively than any other remedy. Hiccough, which is sometimes very distressing, and is often indicative of approaching meteorism and collapse, may be arrested by an ounce of the following mixture, repeated every hour :—

R̄	Liq. trinitrini (1 per cent.)	...	...	℥ viii.
	Spt. chloroformi	...	...	5 i.
	Aq. ...	...	...	ad 5 iv. M.

Alarming hæmorrhage from the bowel may take place at a very



early period of the disease. It is, however, a comparatively infrequent complication, although there are few cases of amœbic dysentery in which ulceration does not, at some time or other, involve a blood-vessel of moderate size. As a rule, the true nature of the condition is easily apparent, but serious hæmorrhage may occur without the passage of blood by the rectum.

When hæmorrhage supervenes the patient should be kept at absolute rest, and if not already under the influence of morphia a full dose should be injected hypodermically. All nourishment, except sips of iced water, should be withheld; and 15 minims of adrenalin chloride solution (1 in 1,000) should be given by the mouth, and repeated at intervals of half an hour as long as may be necessary. If collapse appears to be imminent, resort must be had to stimulants, or to ether and strychnia. Shock and prostration, due to hæmorrhage or to other causes, are effectively combated by the subcutaneous injection of normal saline solution. When this is indicated, a transfusion needle, to which a rubber tube and funnel have been attached, is inserted over the pectoral muscle, and a pint of the solution is allowed to flow slowly into the connective tissue below each clavicle.

#### REMEDIES WHICH SHOULD NOT BE GIVEN DURING ACUTE ATTACKS.

*Ipecacuanha*, although sometimes of great value in the chronic stages of amœbic dysentery, is inadmissible during acute exacerbations. It is especially contra-indicated when the patient is anæmic and enfeebled, when there is high fever, and when there is a tendency to sickness; for in such circumstances, accentuation of all the symptoms, with consequent prostration and collapse, are liable to follow its administration. MUSGRAVE states that, in Manila, he saw at least three cases in which death was directly

attributed to the improper use of ipecacuanha ; and most tropical physicians will agree that this was by no means an uncommon experience.

*Astringents.*—As the object of treatment is to promote rather than to diminish the intestinal secretions, astringents should never be given in acute amœbic dysentery. They invariably fail to check the distressing efforts at defæcation, and by inducing retention of the intestinal contents, they occasionally give rise to very serious symptoms. The recently introduced tannin derivatives, tannigen, tannoform, &c., which are stated to pass unchanged through the stomach, and are, doubtless, effective remedies in many other conditions, appear to be even more unsuitable than catechu, hæmatoxylin, and the older astringents of the Pharmacopœia, for they undoubtedly exercise a more powerful influence on secretion, and, consequently, on assimilation and absorption.

*Intestinal Antiseptics.*—The reputed intestinal germicides almost invariably do harm ; and, although the opportunity would seem to be a favourable one, attempts to arrest the symptoms, and to cut short the progress of amœbic dysentery in its earlier and more acute stages by the energetic use of intestinal antiseptics invariably end in failure. Formerly, tropical physicians made it a routine practice to treat all cases of acute dysentery by large doses of the combination of free chlorine and quinine, which was suggested by Professor BURNEY YEO, and which has proved a valuable remedy in typhoid and many other conditions ; but, although the patient generally experienced some benefit from the relief of flatulence and distension, the mixture had no effect in allaying the pain or in checking the urgency of the rectal symptoms. The antiseptic is, in fact, unable to survive the long passage of the alimentary canal, and it certainly fails to check the development of entamœbæ. Even after much larger doses than those recommended by YEO, the

characteristic odour of chlorine can never be detected in the dejecta, and the vitality of the organisms remains unaffected.

Experience with other intestinal antiseptics has been equally disappointing. Salol, benzosol, and acetozone, which are largely used in the treatment of chronic amœbic dysentery, and are, indeed, considered by many authorities to be superior to any other remedy, are badly tolerated in the acute stages of the disorder. Prescribed in large doses, they invariably upset the digestion, and increase the severity of the symptoms; when ordered in small quantities, they are inert. It is highly improbable, however, that there is any real difference in the therapeutic action of intestinal germicides at different periods in the course of amœbic dysentery; and their failure in the acute stage is, doubtless, attributable to the greater irritability of the stomach, and to the fact that comparatively lengthened administration is necessary for their action to become apparent.

*Antiseptic irrigation* of the bowel should not be attempted during an exacerbation of amœbic dysentery. After the colon has been cleansed by a preliminary douche of warm boracic solution, further direct medication is best deferred until fever and other acute symptoms have subsided; and local treatment should be restricted to soothing injections of small quantities of starch or mucilage. Even these remedies are of questionable value; for, although they relieve tenesmus and induce a marked sense of comfort, it is undoubtedly true that, in acute dysentery, reflex vomiting and other symptoms of severe gastric disturbance frequently originate in the use of rectal injections.

The general management of the acute phases of amœbic dysentery may be summed up in the statement that the best results are obtained by the simplest measures. If during exacerbations the patient is kept at rest, carefully fed, and treated with small doses of

calomel and opium, the periodic crises are notably of shorter duration and less intensity than when a multiplicity of remedies is employed. Energetic measures, or, in other words, the simultaneous administration of powerful antiseptics, *per os* and *per rectum*, and combinations of antidysenteric drugs with active cholagogue purgatives, have naturally passed into disuse; whilst sedatives, such as opium and morphia, disparaged and condemned by the older authorities, are now regarded as almost indispensable aids to treatment.

## CHAPTER XIX.

## THE TREATMENT OF CHRONIC AMŒBIC DYSENTERY.

*General.*

WITH the subsidence of the marked symptoms characteristic of invasion and relapse, amœbic dysentery passes into its chronic or latent stages, and an entirely different line of treatment is now indicated ; but although, as in the acute form of the disorder, considerable modifications may be necessary to meet the varying requirements of individual cases, the management of the condition is again based on definite general principles. As a rule, expectant therapeutics are now abandoned in favour of specific remedies ; active medication—internal and local—is undertaken ; sedatives and anodynes are withheld ; the aid of a strict dietetic *régime* is invoked ; and remedial measures generally are directed to the extermination of the specific parasites. When the disease is of some duration, these organisms, as might be anticipated, are firmly established ; and notwithstanding the fact that the virulence of the infection tends gradually to diminish and natural resistance to increase, a prolonged course of treatment is, almost invariably, essential to a cure.

To a great extent, moreover, the principles of treatment are unaffected by the clinical condition. Necessarily, symptoms vary considerably ; in a certain proportion of cases they are moderately acute, whilst in others they may be almost imperceptible ; but,

whether the course of the disorder has been long or short, whether it has been attended by numerous and severe exacerbations, or whether the manifestations of infection are of a mild and insidious type, the indications for the treatment of chronic amœbic dysentery are always the same.

They are, first, to arrest the development of *entamœbæ* and the consequent destruction of the intestinal walls; secondly, to maintain the general nutrition and to inhibit systemic toxæmia; and, thirdly, to prevent serious complications, and more especially the formation of metastatic abscesses.

These objects are best attained by maintenance of the general health and nutrition, by careful regulation of the diet, by precautions against chill and other possible causes of relapse, and by the administration of antidyenteric and germicide remedies. Apart from specific treatment, the relative importance of these measures varies with circumstances; in the tropics, the question of nutrition generally presents the most serious difficulties, whilst in cold climates the danger of chill is usually the source of greatest anxiety.

When a patient suffering from chronic amœbic dysentery applies for treatment, a history of the symptoms, with special reference to the mode of onset, should be obtained; and the condition of the intestines, the liver and the dejecta should at the same time be carefully investigated. In this way, important information may almost invariably be gained as to the position, the extent and the nature of the lesions. The physical deterioration, the progress of emaciation, the degree of anæmia, and the presence of toxæmia, if any, should also be noted; a weighing machine should be provided, and a record of the weight should be made once or twice a week.

The question of clothing requires particular attention. When treatment is carried out in a cold climate, woollen garments should be worn next the skin by day and by night; and special precau-



tions should be taken against changes of temperature. It is important to keep the hands and feet warm; and recreations which involve exposure to cold, such as motor-driving, fishing, boating, &c., should be forbidden. Bathing must be restricted to a hot bath every second or third night at bed-time; warm baths during the day are unadvisable.

In the tropics, also, the possibility of cold must not be overlooked. Light flannels are the most suitable clothing, and an abdominal belt should always be worn. Serious relapses are not infrequently attributed to chills induced by sitting under a punkah; and, especially after bathing, draughts and currents of cool air should be avoided.

It is seldom necessary to send a patient, during treatment, from a cold to a warmer climate; but, in the temperate zone, sudden falls in the thermometer not infrequently correspond to exacerbations of the symptoms; and the question of transferring an invalid to a milder climate may have to be considered. On the other hand, in the tropics, the issue of the disease often depends on a patient being able to come home for treatment; and in the case of Europeans, repatriation is not only generally advisable, but is often essential to cure. Whenever possible, return to a temperate climate should be made a rule of tropical practice; for although treatment can be, and often is, successfully carried out in the endemic centres of the disease, the prospect of permanent relief is greatly enhanced by a complete change of surroundings. Not only can more suitable diet be obtained, but the benefit which accrues from the feeling of being at home is always of marked therapeutic value.

When return has been definitely settled, the patient should go at the earliest opportunity, and, if necessary, hasten his departure in order to arrive at a mild season. It is a mistake to temporize

or to try half measures. Removal to a hill station is unadvisable; for the high sanatoria of the tropics, invaluable as they are in other conditions, are in most cases unsuited to the treatment of chronic dysentery.

Before advising a patient to return to a cold country, it is, however, necessary to ascertain that his circumstances admit of adequate provision being made for comfort on the voyage, and for treatment when he arrives at home. The facilities which invalids from the tropics find at their disposal on reaching England are, too often, inadequate for their requirements. The sick poor have unrivalled opportunities of receiving satisfactory care during illness; so also have the rich, who can afford to pay high charges for treatment in nursing homes; but for the middle classes—who represent, to a large extent, the average tropical patient—little skilled assistance can be obtained at a reasonable cost. Tropical invalids, moreover, require special care, and in most cases special treatment; and if that cannot be procured, it is infinitely better for them to remain in the tropics. Unless the aid which is indispensable to recovery is at his command, the consequences of sending a patient in an advanced stage of amœbic dysentery to Europe are generally disastrous.

Exercise plays a prominent part in the maintenance of the general health while treatment is being carried out; and, whenever it is practicable, some form of outdoor recreation should be advised. During the latent phases of amœbic dysentery rest in bed is generally unnecessary and undesirable; and, although a patient may have to lie up at intervals, general and regular exercise in the open air has a marked influence in preventing toxæmia and promoting ultimate recovery. Over-exertion and fatigue, on the other hand, must be avoided; for there is no more frequent and potent cause of relapse than exhaustion. When the patient is confined

to bed, daily general massage should be practised. In the tropics excessive exposure to the sun often induces a return of acute dysenteric symptoms ; but, provided that the condition warrants it, a game of golf, walking, and, if more active movement is impossible, driving in the morning and evening are important items in the general management of chronic cases.

When treatment is conducted on right lines the results are more satisfactory than might have been anticipated. Cure is seldom radical or unretarded by relapse, but chronic amœbic dysentery is far from being an intractable affection. On the contrary, compared with other progressive intestinal disorders, it is exceptionally amenable to treatment. When the morbid process has not gone too far, the adoption of appropriate measures is almost invariably followed by surprising improvement, and, in many cases, the patient is restored to complete and permanent health. On the other hand, when the disorder is established, neglect or inability to carry out the necessary treatment generally results in chronic invalidism, and, only too frequently, the illness terminates in death.

## CHAPTER XX.

## DIET IN CHRONIC AMŒBIC DYSENTERY.

IN the treatment of chronic amœbic dysentery, as in that of other intestinal diseases, the question of diet occupies a place of pre-eminent importance. The postulates are : First, the food must be sufficiently nutritious to make good the loss of tissue which results from a protracted illness of an exceptionally wasting nature ; secondly, it must be of such a character that the residues of digestion do not act as fresh sources of irritation to an ulcerated and inflamed colon ; thirdly, in order to counteract the tendency to toxæmia, intestinal digestion must be free from excessive putrefaction and fermentation ; and, further, if the development of parasitic entamœbæ is to be checked, an effort must be made to establish permanent acidity in the contents of the lower bowel. It ought, also, to be borne in mind that the necessary *régime* has in most cases to be followed for a considerable length of time, and the food, therefore, should be capable of some variation, and should be tolerably agreeable to the patient.

## MEAT DIETS.

As a rule these indications are best fulfilled by a diet in which meat greatly preponderates. In many cases of chronic amœbic dysentery a course of meat, absolutely without farinaceous food, continued for several weeks, not only affords sufficient nourishment

but acts as a powerful remedial agent ; and the somewhat anomalous type of amœbiasis, usually known as "planters' diarrhœa," to which reference has already been made, and which is regarded by many authorities as a connecting link between dysentery and sprue, is specially benefited by a diet consisting solely of large quantities of meat (see p. 226).

There are several reasons why meat is preferable to a milk diet in dysentery. It is more easily assimilable, the residuum more closely approaches the natural dejecta of an adult, and it is less likely to set up constipation. PAWLOW and others have shown that meat normally excites a greater flow of the gastric and intestinal secretions than any other food ; there is, in consequence, a diminished tendency to fermentation, and there is less delay in peptonization and absorption. Moreover, in the tropics animal food is almost always obtainable, either freshly killed or frozen and imported, in a more or less satisfactory condition.

On the other hand, there are two drawbacks to the employment of meat in chronic amœbic dysentery. The first is that, as considerable quantities have to be taken, a diet in which flesh greatly preponderates is apt after a short time to become distasteful and nauseous ; and the second, that the resultant dejecta are generally alkaline. Frequent changes in the variety and preparation of animal food, however, help to relieve monotony and prevent satiety ; fish, chicken, game, &c., cooked in different ways, may be advantageously substituted for beef and mutton ; and although, as a rule, carbohydrates must be excluded from the diet farinaceous foods in which proteids predominate, such as macaroni and gluten bread, are specially suited to the treatment of amœbic dysentery. Oranges, peaches, apricots, tomatoes, rhubarb, and green vegetables are admissible additions to a meat diet. Glandular tissues such as liver, kidneys, sweetbreads, &c., and all salted or preserved food, should be avoided.

The alkalization of the intestinal contents by a meat diet is an even stronger objection, as it tends to encourage the development of the specific cause of the disease; but, in most cases, it is readily counteracted by intestinal germicides or other antidysenteric remedies. Slight but sufficient acidity may generally be established by ipecacuanha, benzosol, or sulphate of copper (see pp. 235-239); and when a patient is limited to animal food, one or other of these drugs should be taken regularly.

In the tropics as elsewhere, the prolonged consumption of animal proteids and the exclusion of carbohydrates from the diet of healthy men is apt to be followed by derangements of the renal, hepatic, and circulatory systems. It is a remarkable fact, however, that during the treatment of chronic amœbic dysentery these effects are seldom induced; and, after a protracted illness, the quantity of meat which may be taken with impunity for a lengthened period is astonishing. If the supply of fluid is kept up by copious draughts of hot water—a precaution which should never be neglected—the urine rarely shows any marked excess of nitrogen, the liver and kidneys act freely, and gastric efficiency is unimpaired.

Moreover, disordered appetite and unnatural craving for injurious food which are frequent symptoms of the toxæmic stages of chronic amœbic dysentery, are almost invariably alleviated by a diet of meat. The spasms of acute hunger and the irresistible impulse to consume large quantities of food which the patient knows to be deleterious cease, and marked relief is generally afforded to the other gastric neuroses.

The form in which meat should be given necessarily varies with the general condition. In subacute or in advanced and asthenic cases, it may be desirable to confine the patient to bed, and to commence treatment with soups and jellies, or even to restrict the diet to raw meat juice, liquid peptones, &c.; but, in most instances,



rest in bed is unnecessary. It is further imperative that, except in these special cases, all meat should be lightly and plainly cooked. There are many objections to the use of raw meat, not the least serious being the danger—an imminent one in the tropics—of superimposing a *tænia* infection on the disorder under treatment. Preferably, also, meat should be given in solid form. Minced or pounded beef or mutton, or thin slices from a lightly cooked joint, are almost as digestible and infinitely more nutritious than consommés or liquid extracts.

A general rule as to quantity is that as much meat as can be assimilated without discomfort may be allowed; but, in practice, the amount suitable for individual patients must be carefully estimated for each case—the normal body weight, the natural taste or disinclination for animal food, and the effects of the diet being the best guides to a decision. Men of big build and powerful physique, when restricted almost exclusively to animal food, require 2 lb. of fresh meat daily, and even this quantity is seldom sufficient for adequate nutrition for more than ten days or a fortnight. It is, however, for the time, a full allowance; and, except in special circumstances, it should rarely be necessary to exceed it.

Women are generally unable to tolerate much animal food, and nausea is more readily induced by a meat diet than it is in men. A shorter course of treatment is, on the other hand, usually sufficient; and female patients who are not naturally robust, do better on modified meat diets, combined with intestinal germicides, than on a purely proteid *régime*. In such diets, carbohydrates are strictly limited, although eggs and various albuminous compounds, such as solid peptones, casein, gluten, &c., may often be substituted with advantage for animal proteids.

Of late years, considerable advances have been made in the manufacture of these special products, and several of them are

excellently adapted for tropical practice. As an auxiliary to a modified meat diet, somatose, a granular tasteless powder which is soluble in water, easily digested, and, for its bulk, highly nutritious, is one of the most useful of the solid peptones ; whilst, of the casein preparations, the best known are protene, which appears to be practically pure casein ; plasmon, in which there is over 80 per cent. of proteid ; and sanatogen, which is composed of casein and about 5 per cent. of added glycerophosphate of soda. Apart from their alimentary value—casein, bulk for bulk, is more nutritious than meat proteid—these preparations are often of remarkable service in the treatment of the later stages of amœbic dysentery, and are specially effective in counteracting fermentation and checking the absorption of intestinal toxins.

The following is a specimen of a modified meat diet suited to the treatment of an average case of chronic amœbic dysentery :—

7.30 a.m.—Tea, with milk and a little sugar ; no bread. An orange, a few grapes, or a pear.

9 a.m.—Two lightly boiled eggs. Tea or weak coffee and milk ; a limited quantity of toast and butter. If eggs cannot be taken, fresh fish may be substituted ; and protene or sanatogen may be given instead of tea or coffee. No bacon, ham, or preserved fish is allowed.

11.30 a.m.—Ten ounces of clear soup, with plasmon, or some other proteid preparation.

1.30 p.m.—Six ounces of underdone roast beef or mutton, minced beef, chicken, rabbit, calf's head or game, with macaroni, green vegetables, or tomatoes. Any stewed or fresh non-carbohydrate fruit in season. Strawberries and rhubarb are specially suitable. Apollinaris or Perrier water.

5 p.m.—Tea, with a limited quantity of brown bread and butter

7.30 p.m.—Clear or Julienne soup ; a little dry toast. Fresh fish

cooked in any way, but without flour. For convalescents (in addition): A little cold meat, chicken or game. A pear or other fruit in season. Apollinaris or other table water.

10 p.m.—Ten ounces hot water.

In the tropics many of the articles indicated are, of course, unprocurable, but eggs, fowls, and meat can generally be readily obtained, and many tropical fruits, such as papaya, melon, pumelo, rambutans, avocado pears, &c., are excellent substitutes for European varieties. Whenever possible, fresh bael sherbet should be given twice daily, preferably instead of the other nourishment, at 11.30 and 5 p.m.

The exclusively meat diet, which is so effective in cases of "planter's dysentery," involves complete withdrawal of carbohydrates, total abstinence from all stimulants, a copious supply of mineral waters, or, preferably, of hot water, and an abundant diet of meat. The food consists entirely of fish, eggs, meat (principally underdone chops and beefsteaks), without bread, but with small quantities of fruit and green vegetables. If the patient cannot satisfy his appetite by meat alone, as frequently happens, he is told that the only permissible course is to eat more meat, and meat only, until he ceases to be hungry. When plenty of fluid is taken this drastic *régime* may be kept up for a month or more, generally with the best results to the intestinal condition and with little discomfort beyond the annoyance which is caused by a persistent alkaline taste in the mouth—an almost invariable consequence of a purely meat diet.

#### MILK DIETS.

Although, in the treatment of chronic amœbic dysentery meat must always be the diet of preference, it may be advisable in certain circumstances to restrict the patient, temporarily at least,

to a *régime* of which milk is the sole or principal constituent. The residuum from a milk diet, it is true, is bulky, heavy, and apparently unsuited to an inflamed colon, but, in comparison with normal dejecta, it shows a marked diminution in microbic activity and an almost complete lack of putrefaction. In special circumstances, therefore, and in general whenever meat proves unsuitable, milk should be regarded as the first alternative diet; and in these cases it is advisable to begin with milk alone. On such a diet muscular exertion is impossible, and when the patient is taking nothing else he should be strictly confined to bed. Treatment by a diet consisting solely of milk is, however, a procedure which should not be undertaken lightly or without recognition of the fact that a further serious strain is to be thrown on the vital resources. One of the first effects is a marked and occasionally alarming decrease in weight, and the patient generally complains bitterly of insufficiency of nourishment; but, assuming that the milk is of good quality, and that instructions are carefully followed, there is seldom or never any real danger.

On commencing the treatment it is advisable to give a preliminary dose of castor oil, and after the aperient has acted no food except milk is allowed. The usual quantities are: 60 oz. every twenty-four hours during the first three days; 70 oz. during the next three days, and so on until the maximum, 120 oz. every twenty-four hours, is reached. Unless otherwise directed the milk should not be sterilized or boiled; it should be sipped slowly in small quantities or sucked through a straw. In cold weather it should be slightly warmed. No other restrictions are necessary. Exertion must, of course, be avoided; but the patient may be permitted to get up for a short time every morning and evening and occasionally to have a sponge bath. Unless smoking irritates the mouth it should not be stopped, for sudden discontinuance often causes so much discomfort as to interfere with digestion.

During the continuance of a milk diet laxatives are generally necessary, and it is advisable to give a dose of pulv. glycyrrhizæ co. or liquid extract of cascara on alternate days.

The general improvement which is effected in cases of advanced putrefactive dysentery and toxæmia by the substitution of milk for a mixed diet is often very remarkable. Disinclination for food disappears, lassitude gives place to alertness and a sense of *bien-être*, movement is freer and easier, the complexion freshens, the skin becomes firm and elastic, and there is a marked increase in vascular and muscular tone. As the patient progresses, a little fruit—strawberries or grapes for preference—may be permitted, and beef tea, veal broth, or vegetable purée may be added to the food; but as long as milk forms the principal source of nourishment no meat or other solid food should in any circumstances be allowed.

Soured Milk.—In view of recent researches on intestinal toxæmia, and on the germicidal action of lactic acid-forming bacteria, the possibilities of soured milk as a remedial agent have naturally attracted much attention. It is claimed that at least one variety, now generally known as the bacillus of Massol, when swallowed along with milk, passes with it almost directly to the colon and lower bowel, and that it there produces large quantities of fresh lactic acid, with a consequent acidifying and antiseptic effect on the intestinal contents. It is, therefore, argued that, in this so-called Bulgarian milk, we possess a remedy which is specially adapted to the treatment of amœbiasis; but, clinically, the results have been somewhat disappointing, and recent observation indicates that the therapeutic value of the lactic acid fermentation has been greatly exaggerated. It is possible, however, that this conclusion goes too far, and that soured milk has been too hastily discredited as a dietetic remedy in the treatment of chronic amœbic dysentery.

The truth is that, although in at least half of all the instances in which it has been tried, soured milk has failed to exercise any definite germicide or antitoxæmic effect, in a certain proportion of cases it has given excellent results; and when combined with a suitable diet it certainly assists the action of local antiseptic remedies. It is, undoubtedly, often effective in advanced cases of amoebic dysentery, when ulceration and putrefactive change are prominent features; but, on the other hand, it is generally useless in the commoner form of the disease when toxæmia is attended by inefficient carbohydrate digestion.

No doubt, many of the failures have been due to the fact that, in this country at least, it is by no means easy to obtain properly soured milk. Practically all the solid preparations of lactic acid bacilli now on the market are unreliable. Personal experience, moreover, indicates that fresh cultures are also often unsatisfactory; as, in this country at least, it seems impossible to keep up a continuous strain of Massol's bacillus without special cultures; and, if soured milk is prepared in England in the Bulgarian way—by adding a teaspoonful of the previous day's soured milk to fresh scalded milk—it will generally be found after a few transplantations that, although a soured milk is produced, the original and effective bacillus has been replaced by other organisms. It is, therefore, at present unadvisable to attempt the treatment of septic conditions of the lower bowel by this method unless the soured milk is obtained from a dairy which is equipped with a bacteriological laboratory where the proper strains are kept up, and used for cultivation.

The usual method of administration is to give a pint and a half of soured milk daily, in three quantities of half a pint each. At first, food must be restricted, and for the first day or two little or nothing should be taken besides the soured milk and considerable



quantities of water, to each pint of which two teaspoonfuls of milk sugar have been added. During the continuance of the treatment, an ordinary light mixed diet is advisable; carbohydrates, such as sugar, rice, cornflour, &c., ought to be well represented, and meat should be allowed only once a day. A purely vegetable diet is, however, unsuitable; and fat and butter ought to be limited in quantity. No intestinal antiseptics should be given by the mouth, and alcohol in any form is prejudicial to the success of the treatment.

#### ALCOHOL IN CHRONIC AMÆBIC DYSENTERY.

Alcohol is, indeed, essentially antagonistic to the action of most specific remedies; and during active treatment abstinence from all forms of wine and spirits is advisable. In certain cases, however, stimulants may be required; and when there is marked failure of strength, loss of appetite, and depression—a condition which not infrequently follows complete deprivation—it is generally necessary to prescribe alcohol. In such circumstances, limited quantities of cognac, or malt whisky, freely diluted with soda-water, are less likely to be harmful than other forms of stimulant.

## CHAPTER XXI.

## THE TREATMENT OF AMŒBIC DYSENTERY BY DRUGS.

ANTIDYSENTERIC REMEDIES.—There is no subject in the history of therapeutics on which there has been greater diversity of teaching than the treatment of chronic dysentery by internal remedies. To a considerable extent, the conflict of opinion has been in respect of the utility of ipecacuanha; but essential principles and methods have been almost equally in dispute. Moreover, although an endless number and variety of drugs have been employed, there is still no general consensus of authority as to their curative value; and most of the remedies now in use have, on the one hand, been vaunted as specifics by their adherents, while, on the other, they have been condemned as worthless by at least as many detractors.

*Ipecacuanha*.—The tendency on both sides has, no doubt, been to speak too dogmatically; but it is significant that, in spite of much hostile criticism, ipecacuanha has successfully maintained a definite reputation as an antidyenteric for two hundred and fifty years, and that it is still generally regarded as the first remedy to be tried in an ordinary case of chronic amœbic dysentery. It is, indeed, the most important example of a class of drugs which are believed to possess special antidyenteric properties, and which have long been accepted as standard remedies for the disorder.

The truth is that ipecacuanha, although a medicine of great efficacy in certain varieties and phases of dysentery, has very definite

limitations, and that it is actually harmful unless the conditions under which it may be given are clearly recognized. It is, for instance, contra-indicated during acute attacks, or when there is marked elevation of temperature ; it has little, if any, remedial value in bacillary dysentery ; whilst in sprue and other intestinal disorders which are apt to be confused with amœbic infections it is always deleterious. On the other hand, in certain cases of chronic amœbic dysentery, the effect which is produced by full doses of ipecacuanha, properly administered, is often surprising ; and although the encomiums which the drug has received from DELIOUX DE SAVIGNAC, MACLEAN and others are unwarranted, it may fairly be described as a remedy of moderate but definite practical utility.

Originally brought to France from Brazil by PISO, in 1648, and introduced under the name of *Radix antidysenterica*, ipecacuanha immediately gained a remarkable vogue from the circumstance that it was successfully prescribed for the Dauphin ; but it appears to have afterwards fallen into comparative disrepute, for although dysentery was everywhere rife, little more was heard of it in Europe. In India, however, ipecacuanha continued to be employed with more or less success, and Surgeon Docker of the 7th Fusiliers again brought it into prominent notice in 1858 by publishing an important paper in which he showed that at least one cause of failure was the fact that the remedy had been given in insufficient doses.

Another reason for the frequent inefficacy of ipecacuanha is that in hot climates the root is apt to deteriorate, and samples of the drug, especially those which have been kept for some time in powdered form, are often inert. The Brazilian variety of the plant—*Psychotria ipecacuanha*—has, however, been successfully introduced into the Eastern tropics, and the root-bark of this species can generally be obtained in a “recent” condition. When fresh

ipêcacuanha is unprocurable, the liquid extract of the British Pharmacopeia may be used; it keeps well, is fairly active, and is free from most of the disadvantages of the older preparations.

DOCKER, whose mode of administration is still widely used, prescribed the powdered root-bark in 25 or 30-grain doses; but the following modification of the so-called Brazilian method is more effective, and is less apt to induce vomiting.

The patient is temporarily confined to bed, and after a light dinner, consisting only of soup or veal broth, he takes at 9 p.m. half an ounce of castor oil. At 7 a.m. the following morning, a cup of tea with a thin slice of toast may be given, but no breakfast is allowed. At 9.30 a mustard plaster is applied to the epigastrium, and at 10.30, an ounce of decoction of ipêcacuanha is taken, and is repeated every hour for four hours. The decoction is prepared in the following way: A drachm of fresh root bark is bruised and boiled for five minutes in 4 ounces of water; after straining through fine muslin, it is allowed to cool, and 2 drachms of tincture of cinnamon are then added to the decoction.

During the administration of the remedy, the patient lies perfectly still in bed, and takes no food or other liquid; the head is kept low, and talking is strictly prohibited. If nausea supervenes, the medicine is stopped, and the inclination to vomit is resisted as long as possible. An hour and a half after the last dose, a wine-glassful of iced chicken jelly is given, and later a basin of Benger's food may be retained. The treatment should be repeated daily for three days.

Personal experience shows that, if directions are carefully followed, ipêcacuanha given in this way seldom induces vomiting, that no opium is necessary, and that, if fresh root-bark only is used, a satisfactory result is obtained without further medicinal treatment in from 30 to 40 per cent. of all cases. When DOCKER's method is

employed, a bolus of 30 grains of powdered root-bark is administered after a preliminary dose of 30 minims of laudanum; but, although the opium doubtless controls the tendency to nausea, it also arrests the intestinal secretions, and thereby limits the curative action of the ipecacuanha. Moreover, when vomiting does occur, it is of an unusually distressing type, and the experience of most physicians is that the nausea which follows a combination of ipecacuanha and opium is so intense that a patient can rarely be persuaded to make another attempt to take the remedy.

Various procedures have been devised to obtain the antidysenteric action of ipecacuanha without the emetic effect of the drug, and of these continued administration in fractional doses for three or four days is perhaps the most successful. One such method, usually known as LE DANTEC'S, is extensively employed in Cochin China, and has gained a considerable reputation in the French Colonies as an easily tolerated and effective treatment of chronic amœbic dysentery. The ipecacuanha is prescribed in the following way: Successive watery extracts are prepared from 2 drachms of bruised root-bark: (1) By soaking it in 6 ounces of cold water for twenty-four hours; (2) by infusing the root-bark after exhaustion in this way in 6 ounces of boiling water for two hours, and (3) by afterwards boiling it for half an hour in a similar quantity of water. The three solutions are given in their proper order in dessert-spoonful doses on three following days, the whole of one solution being taken each day. During the administration of the remedy, no food except soup, arrowroot, &c., is allowed.

The alkaloids and pharmaceutical preparations of ipecacuanha are much less effective than powdered root-bark, and the so-called de-emetinized ipecacuanha certainly lacks the antidysenteric properties of the entire drug.

*The Effects of Ipecacuanha.*—When successful, the action of

ipecacuanha is at once apparent. In most instances, a copious loose motion of characteristic yellow colour and acid reaction is passed within three or four hours, and the patient experiences a marked sense of relief. Similar discharges, almost entirely free from mucus and blood, are voided during the next two or three days; the intestinal functions gradually become normal, and the patient is soon convalescent. Apart from careful dieting, further treatment is generally unnecessary.

Ipecacuanha doubtless acts by stimulating secretions which are prejudicial to amœbic life in the intestine. A decoction prepared as directed for internal administration, when diluted to 1-100, applied to living entamœbæ on a slide, arrests their movements; but it does so less promptly and effectively than a weak solution, (1-5000) of quinine hydrochlorate—a drug which has no antidysenteric action. Further, it is difficult to see how organisms in the intestinal coats can be destroyed, as in many cases they undoubtedly are, by ipecacuanha, unless there is more than a merely local action, and unless the circulation in the tissues has been materially modified by the addition of an internal secretion.

There are few contra-indications to the use of ipecacuanha. It is true that in pregnancy and other conditions, which are accompanied by severe vomiting, the remedy may aggravate the symptoms, and that, when there is marked anæmia or prostration, the administration of ipecacuanha may be attended by some risk; but personal experience indicates that it can be given to young children and delicate subjects without the slightest danger. In a recent case of chronic amœbic dysentery complicated with severe and persistent vomiting of hysterical type, decoction of ipecacuanha was retained without difficulty, and the patient who, in the tropics, had been seriously ill at intervals for fifteen months, made an excellent recovery.



*Other Antidysenteric Remedies.*—Definite antidysenteric virtues have been attributed to many other tropical products of vegetable origin; but although some of them are useful as alternatives to ipecacuanha, none are equal, and most are distinctly inferior to that drug. Four, however, deserve a word of notice; they are simaruba, ailanthus, kho-sam, and the fruit of the bael tree.

*Simaruba*, the root-bark of the mountain damson (*Simaruba officinalis*) is a popular remedy in Java and the East Indies, and is officially recognized in the Dutch and other Continental pharmacopœias. Like ipecacuanha, it ought to be freshly prepared. The usual method of administration is to soak  $\frac{1}{2}$  oz. of root-bark in a pint of boiling water for a quarter of an hour, the whole of the infusion being taken in doses of 2 or 3 oz., at short intervals, within twenty-four hours. *Simaruba* occasionally induces nausea, but in most cases it may be continued for a week or more without ill-effect; patients like its bitter and slightly astringent taste, and the antidysenteric action is sometimes very remarkable. The infusion may also be used as an intestinal injection.

*Ailanthus*, although frequently confused with *simaruba*, has, in fact, no connection with that product. It is the root-bark of *Ailanthus glandulosa*, a terebinthine tree, indigenous in the Far East; and it has been used by the Chinese as a remedy for chronic dysentery from time immemorial. Native physicians, indeed, regard *ailanthus* as a far more reliable antidysenteric than ipecacuanha or any other drug; and personal experience is to the effect that, in some instances at least, an infusion of *ailanthus* prepared by macerating 2 oz. of root-bark in  $\frac{1}{2}$  pint of boiling water is a medicine of great efficacy. Two ounces of the infusion are taken at intervals of not less than six or eight hours.

In large doses *ailanthus* has marked depressant and nauseating effects, and as it has also a cumulative action caution must be

exercised in continuing the drug for more than two or three days. MATIGNON, who regards it as a specific in chronic amœbic dysentery, records an instance in which an overdose of infusion of ailanthus was followed by a fatal result.

*Kho-sam*.—The dried seed of *Brucea sumatrana*—generally known by the Japanese name of kho-sam—enjoys a wide celebrity in the Eastern tropics as an antidysenteric, and highly successful results have recently been obtained by its use in the treatment of chronic amœbic dysentery. The fruit is a greyish almond-like nut, and the kernel contains a large quantity of a powerful cholagogue and emetic alkaloid—chosamine. MOUGEOT, of Saigon, who treated 879 cases by kho-sam, states that it was successful in no fewer than 871 instances, whilst SCHNEIDER, of Teheran, Professor LEMOINE, of Val-de-Grâce, and many others who have investigated its therapeutic properties bear emphatic testimony in its favour. The drug can now be obtained in the form of compressed tablets, known as Elkossam, each of which represents one kernel. Five or six tablets are taken daily.

*Bael Fruit*.—The bael (*Aegle marmelos*) flourishes abundantly in Bengal and Southern India, and the fruit is prized throughout the tropics as an antidysenteric and antiscorbutic remedy of great value. The pulp of the ripe bael may be sliced and eaten with pounded sugar; but the best effects are obtained by preparing a “sherbet” from the unripe fruit in the following way: The pulp is cut into cubes of an inch square, and placed with a little white sugar in an earthenware jug. To this a pint of boiling water is added, and the contents after being well stirred are allowed to cool. This infusion or sherbet is drunk *ad libitum*, from 30 to 60 oz. being taken in the twenty-four hours. Bael is an excellent tonic and restorative at all periods of amœbic dysentery, but is specially valuable during convalescence and when the patient is returning to a normal diet.

**PROTOZOAN GERMICIDES.**—Several of the synthetic remedies which are known as internal germicides, and which have proved useful as intestinal antiseptics in typhoid and similar conditions, have of late years been largely employed in the treatment of chronic amœbic dysentery. Most of them exercise a directly destructive influence on entamœbæ, and as they seldom induce nausea, they are excellently adapted for the treatment of cases in which ipecacuanha is badly tolerated.

Of these drugs, benzosol, salol, and acetozone are the most reliable remedies for all varieties of protozoan dysentery. Their marked antiseptic properties are but little affected by their passage through the upper part of the intestine, and in the colon they still retain at least the greater part of their original activity. Opinions differ as to their relative merits, but a considerable personal experience indicates that benzosol is the most promising and generally useful of the three. Apart from its undoubted efficacy as a germicide, it produces no constitutional or local reaction, and its marked therapeutic value in the treatment of intestinal amœbiasis has been abundantly confirmed.

*Benzosol* (benzoate of guaiacol) occurs in minute acicular white crystals, which, although soluble in chloroform and hot alcohol, are almost insoluble in water. On coming in contact with the gastric juice it is saponified; the benzoic acid disappears from the molecule, and the drug ultimately reaches the colon as uncombined guaiacol. The doses recommended in therapeutical guide-books are much too small; to produce a definite antiseptic action in the intestine, benzosol must be ordered in substantial quantities—40 to 60 gr. daily. Five-grain doses are quite ineffective for an adult; and the best results are obtained by giving 20 gr. in the morning, 10 gr. in the middle of the day, and 20 gr. in the evening. Tablets of benzosol are apt to become hard and insoluble, and it is advisable to prescribe the remedy in cachet.

Benzosol has slightly laxative properties, and at first it occasionally induces marked looseness of the bowels; but, in the treatment of amœbic dysentery, this is seldom disadvantageous; and although the action of the remedy must be carefully watched, a little diarrhœa is beneficial rather than otherwise. The dejecta passed after full doses have nothing of the appearance of ipecacuanha motions; they are dark and bilious looking; they seldom contain mucus or blood; and the reaction is strongly acid.

Benzosol is especially suitable for the treatment of the latent phases of amœbic dysentery, as during its administration rest in bed is generally unnecessary. After ascertaining that it agrees with the patient, benzosol ought to be continued for a month or six weeks without interruption; and then, after a pause of two or three weeks, it may be resumed if necessary; but, in many cases, the dysenteric symptoms entirely disappear after a short course of the drug, and there are no subsequent recrudescences.

*Benzoyl-acetyl-peroxide*—a synthetic preparation which may be regarded as hydrogen peroxide, in which half of the hydrogen has been replaced by benzoyl, and the other half by acetyl—is a favourite remedy in the garrison hospitals of the U. S. Government in Manila. It is commended as an exceptionally powerful intestinal germicide by Drs. STRONG and FREER; and an important point in its favour is that, although in some instances it has been given in larger doses than are necessary for antiseptic purposes, no unfavourable physiological effects have been observed.

Benzoyl-acetyl-peroxide is used both internally and locally. Five grains are given by the mouth, in a celloidin or keratin capsule, three times a day; and, once daily, two quarts of 1-1000 dilution are allowed to flow into the colon by a long rectal tube. The treatment is continued for two or three weeks. A solution of benzoyl-acetyl-peroxide of similar strength may be used at the same

time instead of drinking water; and patients who have taken it *ad libitum* in this way for several weeks have found it an effective and agreeable beverage. The recorded results of this method of treatment are excellent; but at present the drug is often difficult to obtain; and, in the tropics at least, it is an unstable compound. It is, moreover, too expensive for general use.

*Salol* (phenyl-salicylate) has been recommended<sup>1</sup> by numerous writers on amœbic dysentery as a useful intestinal antiseptic; and, in many cases, it undoubtedly exercises a marked beneficial influence. It appears, however, to act on the bacteria of the alimentary tract more effectively than on parasitic protozoa; and compared with benzosol it has many drawbacks. Like that drug, it must be given in full doses in order to secure its germicide action; and, as the phenyl radicle is excreted by the urinary tract, nephritis is apt to be set up unless the kidneys are perfectly sound and capable of withstanding a considerable strain on their powers of elimination. The effects of salol, moreover, are less marked in the colon than in the small intestine; and although inferior as a germicide to benzosol it cannot with safety be continued for so long.

Cases in which the dejecta are extremely offensive and putrid often do better on salol than on any other drug; and when its use appears to be desirable, at least 15 gr. should be ordered three times a day. When the patient is taking solid food, even that quantity is insufficient to secure moderate asepsis; and unless there is evidence of intolerance the dose in such cases should be increased to 20 gr. Salol is generally ordered in cachet, but it appears to be more effective when prescribed as an emulsion. The following formula, suggested by MARTINDALE, provides an excellent and con-

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<sup>1</sup> See R. Strong and others: *Bulletin of the Biological Laboratory*. Manila, 1904.



venient intestinal disinfectant for routine use: Dissolve 20 gr. of salol in a fluid drachm of liquid paraffin by the aid of heat: while hot, triturate vigorously, and add 30 gr. of powdered gum acacia, afterwards making up to 1 fluid ounce with distilled water.

*Salophen* has been recommended as a satisfactory substitute for salol; and, as it contains a smaller proportion of phenyl, it seldom or never acts as an irritant to the renal epithelium. Like salol, it is unaffected by the gastric juice, and dissolves only when it meets the pancreatic ferments in the alkaline tract of the small intestine. *Salophen* has gained a considerable reputation in the Dutch East Indies as a remedy for typhoid and other septic conditions of the intestine, and has recently been largely prescribed for amœbic infections. A limited personal experience is, on the whole, favourable. Not less than 30-gr. doses should be ordered.

*Acetozone* (benzoyl-acetyl-peroxide) has also been extensively employed in America and in the Philippine Islands. Like most of the other synthetic remedies, it is but sparingly soluble in water and in acid solutions, although in the small intestine it splits up into acetyl hydrogen and benzoyl hydrogen, both of which are powerful germicides. MUSGRAVE states<sup>2</sup> that the best results are obtained by prescribing large quantities of a dilute solution of acetozone to be drunk freely at intervals during the day. For this purpose he recommends aerated water as being more palatable and convenient for tropical use, and says that three or four pints of solution of acetozone in soda water (1-2,500 or 1-5,000) may be taken every twenty-four hours.

There is some difference of opinion as to dosage, but it is

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<sup>2</sup> W. E. Musgrave, "Treatment of Amœbic Dysentery in the Tropics," Manila, *Bulletin of the Biological Laboratory*, 1904.



generally agreed that acetozone should always be given either in weak solution or with large potations of water. Thirty grains dissolved in four pints of water were given by LLEWELLYN<sup>3</sup> without ill effect, but CHARLES WRAY, who ordered it to be taken in capsules, followed by copious draughts of water, considered<sup>4</sup> that  $\frac{1}{2}$  grain was a sufficient dose. MUSGRAVE, who has used it extensively, states that he has seen unfavourable symptoms follow the administration of acetozone in celloidin-coated capsules, and he believes that they were due to premature rupture of imperfect coverings, with consequent liberation of the drug in a concentrated form in the stomach.

On the whole, acetozone may be regarded as a reliable protozoan germicide, but one which must be used with great circumspection. It should only be prescribed in very dilute solution, and in doses of not more than 5 grains. My own experience is to the effect that, unless given with an aperient, acetozone is somewhat constipating—a distinct disadvantage. It is also very expensive.

*Oil of Turpentine.*—In the tropics these synthetic germicides, although rapidly coming into general use, are frequently unprocureable, and it may be necessary to have recourse to simple remedies. *Oil of turpentine* often gives excellent results in the treatment of chronic amœbic dysentery; and, as Sir JOSEPH FAYRER pointed out many years ago,<sup>5</sup> it is specially useful in the more chronic forms of the disease, when the type of ulceration is indolent and extensive.

The administration of turpentine is attended by considerable difficulty. Like other intestinal antiseptics, it must be given in full

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<sup>3</sup> Llewellyn, *Australian Medical Gazette*, February 20, 1905.

<sup>4</sup> *Medical Annual*, 1909, p. 387. Wright, Bristol.

<sup>5</sup> "Tropical Dysentery and Chronic Diarrhœa." Churchill, 1881.

doses, 30, 40 or even 60 minims, three or four times daily ; and its pungent odour and acrid taste are serious disadvantages. Many patients, indeed, are quite unable to take turpentine in any form. Capsules containing the liquid oil either become hard and insoluble or they rupture too readily ; and in hot climates they are specially unsatisfactory. An emulsion prepared as follows may, however, often be taken without difficulty : 30 grains of powdered gum acacia are rubbed up, first with a fluid drachm of turpentine and afterwards with an equal quantity of water, the mixture being gradually made up to an ounce by trituration with *mist. amygdalæ*. Half an ounce to an ounce is a suitable dose.

When large doses of turpentine can be tolerated, the germicide action is at least equal to that of benzosol, and the soothing and healing effects which it produces are often very remarkable. In hæmorrhagic dysentery, turpentine generally acts promptly and satisfactorily as a hæmostatic ; and in malignant cases it may be instrumental in saving life by arresting the tendency to tympanites and meteorism. Combined with castor oil it is an effective remedy in those cases of chronic amœbic dysentery in which constipation and the passage of large masses of mucus are prominent symptoms.

A better effect is secured by administering turpentine in single large doses than by giving it frequently in small quantities, and whenever possible it should be ordered in that way. There are few contra-indications to its use, but it is always inadmissible when there is albuminuria.

*Sulphate of Copper and Opium.*—In certain cases of chronic amœbic dysentery highly satisfactory results are obtained by the use of sulphate of copper and opium. The combination is specially adapted to the treatment of that latent form of the disorder to which attention has already been directed and which is generally known as “planters’ dysentery.” The following formula may be used :—

R	Cupri sulph.	...	...	...	$\frac{1}{4}$ gr.	
	Pulv. opii....	...	...	...	$\frac{1}{2}$ "	
	Massa paraffini	...	...	...	2 "	Ft. pil.

Such a pill should be taken three times daily after food, and the diet should be limited almost entirely to meat. In these doses, sulphate of copper rarely produces any feeling of nausea and in cases of long standing surprising cures are often effected. Without the sulphate of copper or without the opium the remedy is of little value, and the remarkable efficacy of the pill is due to the combination of the drugs.

*Saline Aperients.*—The treatment of acute dysentery by saline aperients, originally introduced by French physicians about the middle of last century, has now for many years been a general and approved method of practice. DUJARDIN-BEAUMETZ, writing of acute tropical dysentery (which, however, was probably of the bacillary variety) said, "When we see bile again in the dejecta the patient is cured"; and he believed that this object could be best attained by the regular and continued administration of the sulphates of magnesia and soda. In India the saline treatment of acute dysentery has always been favoured, and of late years the method has also been largely utilized in the chronic stages of the amœbic variety of the disease.

Here, however, the results have been by no means always satisfactory. It is undoubtedly true that Epsom and Glauber's salts may be given with marked benefit; but the action of salines is extremely irregular and uncertain; and they are unsuitable for routine employment. Given in small and frequently repeated doses, salines render the contents of the alimentary canal strongly alkaline, and consequently promote a rapid growth of amœbic organisms, with a corresponding increase in the dysenteric symptoms.

In certain cases, however, they may prove to be of great service.

The beneficial results which follow their use appear to be due to their purgative effects, and to their action in dissolving the viscid mucus which adheres to the surface of the colon. Not only is a protozoan breeding-ground of exceptional fertility frequently broken down and removed, but the inflamed mucosa is made more readily available to the remedial action of intestinal germicides. For this reason salines are likely to be of utility when local medication is employed.

Aperients of all sorts, and particularly alkaline sulphates, often prove effective in cases in which dysenteric symptoms are combined with chronic dyspepsia, portal congestion, and functional derangement of the liver; and they are generally indicated in the chronic amœbic dysentery of plethoric and alcoholic subjects. Many of these cases do well when a course of treatment at a mineral spa is undertaken; and salines are systematically employed in combination with the Plombières system of cure. In cases of marked anæmia, depletion, and emaciation, they are contra-indicated.

When prescribed in chronic amœbic dysentery, salines must generally be continued for a considerable time; and one of the best methods of administration is to order a drachm of sulphate of soda, in 6 oz. of hot water, three times a day before food. After a week or ten days, the midday draught is omitted; and ultimately no more than one dose in the early morning is necessary.

## CHAPTER XXII.

## LOCAL MEDICATION.

THE direct application of germicide remedies to the inflamed and ulcerated intestine is of special importance in the chronic stages of amœbic dysentery. Indolent sores and putrid centres of toxin formation are frequently restored to healthy action by means of rectal injections after all other methods of treatment have failed; and the specific micro-organisms—on which the persistence of the disease depends—are more effectively destroyed in this way than by any other form of medication.

Doubts have been expressed as to the utility of germicide douches on the ground that anatomical and physical conditions make it impossible for rectal injections to reach the seat of disease in the colon, and that, in any case, these solutions cannot possibly affect *entamœbæ* which are developing in the sub-mucosa and the deeper tissues of the intestinal wall. But it has been repeatedly shown by skiagrams, and in many other ways, that local applications properly introduced encounter no serious obstacle until they arrive at the ileo-cæcal valve; and practical results abundantly attest their efficacy and value. No therapeutical fact is more fully confirmed than that deeply-seated organisms may be destroyed by flushing the colon with suitable germicides, and that direct medication is the most rapid and effective method of dealing with protracted and obstinate amœbic infections.

The local treatment of chronic amœbic dysentery generally

necessitates the administration of at least ten or twelve intestinal douches—one or two being given daily—and as during this period the diet must be carefully regulated, and the bowel prepared for the reception of each injection, the patient should, if possible, be placed in a nursing home. To a great extent success is dependent on efficiency of method and technique; and the best results can only be attained when continuous attention is given to the details of treatment.

Practice, moreover, must be regulated by the general condition. In most cases absolute rest in bed is unnecessary, and a certain amount of movement and distraction is desirable. After irrigation the patient may sit up in an easy chair, or move about from room to room. In exceptionally mild cases, germicide douches may be employed without interference with the usual occupations, but active movement or exertion, except in the intervals of local treatment, should be forbidden. Absolute rules for this as for other details of treatment are, however, undesirable, and each case should be treated on its own merits.

The introduction of a germicide solution is best effected by means of a soft but substantial rubber tube, one and a half to two yards in length, attached to a glass reservoir of two quarts capacity, from which, solely by force of gravity, fluid may flow freely and steadily into the intestine. On account of their tendency to excite peristalsis, Higginson's and other forms of pump syringe are unsuitable; funnels are apt to admit air; and rubber reservoirs decompose and are difficult to keep clean. The rectal portion of the tube, although flexible, must be sufficiently rigid to keep a direct course to the upper curve of the sigmoid flexure under the gentle force which is necessary to overcome the obstruction offered by an infiltrated and often constricted passage; the nozzle should be rounded, with only one opening at the extreme tip; and the



body of the tube should be perfectly smooth, of uniform calibre, and not more than five-eighths of an inch in diameter.

Suitable irrigation tubes are difficult to obtain, and although a serviceable appliance may be fitted up by connecting a soft rubber pipe to a stomach tube, a special apparatus is desirable. An intestinal irrigator has been constructed for me by Messrs. Allen and Hanbury which has the following advantages: It can be thoroughly and rapidly sterilized; the distal end is hardened and slightly contracted, so that if it becomes clogged with mucus or other matter, it may be readily cleared by a little manipulation and compression of the tube; it cannot kink or turn back in the bowel; and the flow of fluid into the intestine may be accurately observed and regulated.

Before the administration of a germicide injection the lower intestine should be washed out by a preliminary douche of 50 or 60 oz. of warm water, or a weak solution of boric acid (1 gr. to the ounce). For cleansing purposes mucilaginous vegetable infusions, such as linseed, are unsuitable; and as soap, bicarbonate of soda and other alkalines may counteract subsequent acidity they should also be avoided.

While an injection is being administered the relations of the rectum to the other abdominal viscera are important. The pelvis should be raised on a hard pillow 8 or 10 in. above the level of the bed, and the patient should be placed across the elevation in the left prone position; that is to say, he should lie on the left side with the right thigh flexed on the abdomen, and the face and chest turned down to the mattress. In this attitude the highest part of the colon—the splenic flexure—will be 5 or 6 in., and the lowest—the hepatic flexure—8 or 9 in. below the sigmo-rectal junction. The tube, well lubricated with unmedicated vaseline, is then carefully introduced as far as it will go without undue pressure, and

30 or 40 oz. of solution, warmed to 96°—98°, are allowed to flow steadily into the bowel. During the operation the patient must keep perfectly still, and the same position should be maintained for five minutes after the injection.

Given in this way, a remedial application readily penetrates to all parts of the colon, and is usually retained without difficulty; whereas, if the patient is rolled or swayed about, as is often recommended, spasm and the accumulation of flatus are generally induced, and the desire to evacuate the injection becomes uncontrollable.

Although the left prone attitude is generally preferred, many physicians advocate the dorsal or the knee-elbow positions, and provided the pelvis is well raised they are almost equally satisfactory. In cases where the intestinal reflexes are abnormally excitable and the mucosa hyper-sensitive, rectal irritability may be overcome by raising the end of the bed 18 in., or if that is ineffective by placing the patient in the Trendelenburg position; but in ordinary circumstances these proceedings are unnecessary.

Flatulent accumulations in the alimentary tract are by far the most frequent cause of intolerance of injections. If they are not brought away by the preliminary douche, intestinal gases may sometimes be successfully expelled by abdominal massage, or by giving a second douche of normal saline solution containing 20 m. of liquor opii sedativus before the injection. In cases of persistent fermentation and irritability, *Pil. asafoetidæ* co. is a useful and reliable remedy. The rectal tube and connection should be freed from air before introduction.

Even when every precaution is observed, a certain amount of reflex spasm is almost invariably excited by the inflow of fluid. In some instances a rapid stream seems to be less irritant than a slow trickle; in others, only complete cessation can avert immediate expulsion of the injection. In such circumstances the condi-

tions best suited to each case must be determined by changes in manipulation, in the strength and temperature of the injection, or in the position of the patient. TUTTLE states that he treated amœbic dysentery successfully and with almost complete freedom from discomfort or spasm by large enemias of ice-water; and as he had previously claimed that cold—which affects free-living amœbæ scarcely at all—was fatal to parasitic forms he believed that the germicide action was a result of the low temperature. MUSGRAVE, HARRIS and others who agree to the soothing effects of cold, have, however, shown that frozen dysenteric dejecta, when thawed and injected into cats, still induce true amœbic dysentery.

There is, moreover, great variation in capacity to tolerate large quantities of fluid. Most patients are able to retain three pints, but four or even more are frequently introduced without causing the slightest inconvenience. The female abdomen is, naturally, more tolerant than the male. The point is of some importance, for the local medication of chronic amœbic dysentery can be satisfactorily carried out only by copious quantities of fluid, and it should be an invariable rule of practice to make injections as large as they can be borne.

Numerous experiments have been undertaken to test the exact germicide values of different preparations, but *in vitro* results are by no means reliable guides to treatment, and clinical experience indicates that the selection of a remedy presents fewer difficulties and is of less practical importance than efficiency of technique and method in administration. Provided it is an active germicide, constitutionally innocuous and properly administered, success may be attained by almost any one of a large number of drugs; but, in practice, solutions of the salts of silver and of quinine are generally regarded as the most useful preparations.

*Silver compounds.*—On account of their unirritating effects the

proteid compounds of silver are preferable to inorganic salts of the metal ; and personal experience has shown that argyrol—a soluble combination of silver with a wheat proteid—is better adapted to the local treatment of chronic amœbic dysentery than any other remedy. After a preliminary cleansing douche, 2 pints or more of a freshly prepared 1 per cent. solution of argyrol at 95° to 98° F. are allowed to flow into the colon and are retained as long as possible. This injection should be repeated once daily for ten days or a fortnight, and if it is well borne the strength of the solution may be gradually increased to 2 per cent. and the quantity to 3 or 4 pints.

When properly administered, argyrol injections cause little irritation, and practically no pain. Patients generally say that at first only a pleasant feeling of warmth is induced by the inflow of the solution ; but when the higher strengths are employed and ulceration is recent, there may be a little sharp tingling. In respect of pain, however, argyrol compares very favourably with the nitrate and other salts of silver. Protargol—in which there is a much smaller proportion of silver—is more liable to cause irritation ; and, relatively to argyrol, is unsatisfactory and ineffective.

*Solutions of quinine*, originally proposed by LÖSCH in 1875, have been extensively employed in the local treatment of amœbic dysentery, and when used with discrimination, give excellent results. HARRIS claims that the bisulphate has a higher germicide value than any of the other preparations of quinine, but its special efficacy is more than doubtful. The fact is that all the salts of quinine are almost equally potent, and that the rapidity and extent of their action depend, in a great measure, on the acidity of the solution. Insoluble salts dissolved in a slight excess of acid are more effective, and should always be employed in preference to soluble preparations of quinine.

High concentrations of quinine generally cause considerable

pain, and not infrequently a strong injection is followed by acute suffering. In no case should the proportion exceed 1 in 750, and this strength should only be gradually reached. Twenty grains of bisulphate of quinine, dissolved in 40 min. of dilute sulphuric acid, with 60 ounces of warm water (approximately 1 in 1,500), make a suitable solution for the first injection, the quinine being increased by 5 grains every third day. Like other germicide douches, the solution should be introduced at a temperature of 96° F. or a little over; and if there is pain, a hypodermic injection of morphia should be given. The insertion of a cocaine suppository ( $\frac{1}{2}$  grain) five minutes before a quinine injection is recommended by many physicians.

The bionomic relation of intestinal bacteria to entamœbæ has a definite therapeutic interest, and the germicidal effects of various solutions on organisms growing in symbiosis have been studied by several observers. THOMAS<sup>1</sup> obtained the following results with symbiotic cultures of amœbæ and reputed spirilla of Asiatic cholera:—

(1) Boric acid, eucalyptus, ichthyol, and oil of cassia had little or no effect on either organism. HARRIS has also shown that strong solutions of boric acid cause a temporary cessation of vitality but have no destructive action.

(2) Tannic acid 1 in 100, copper sulphate 1 in 2,000, potassium permanganate 1 in 4,000, and bisulphate of quinine 1 in 1,000, partially destroyed both amœbic organisms and spirilla.

(3) Potassium permanganate 1 in 2,000, quinine bisulphate 1 in 500, nitrate of silver 1 in 2,000, argyrol 1 in 500, and protargol 1 in 500, promptly killed the spirilla, but failed to affect some of the amœbæ. All life was, however, destroyed by doubling the strength of these solutions.

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<sup>1</sup> *American Journal of Medical Sciences*, January, 1906.

(4) Thymol 1 in 2,500 destroyed the amœbæ without affecting the spirilla.

*Other germicides.*—General experience indicates that, in practice, excellent results may be obtained by the use of solutions of permanganate of potash, of sulphate of copper, and of thymol in the strengths indicated. The two latter, however, occasionally give rise to considerable pain; and the residues left by permanganate injections simulate decomposed blood so closely that the intestinal condition is often obscured.

Personal observation has, further, confirmed the value of strong solutions of creosote in the treatment of hæmorrhagic amœbic dysentery, advocated<sup>2</sup> by MM. CHANTEMESSE and RODRIGUEZ. In their case, that of a patient from Guatemala, whose motions consisted of almost pure blood, and contained large numbers of *Entamœba histolytica*, douches of creosote, of a strength of 5 grammes to a litre of water ( $\frac{1}{2}$  per cent.), rapidly effected a complete cure. In a somewhat similar case, in which considerable quantities of blood and mucus were passed periodically at intervals of two or three months, and which had resisted treatment by ipecacuanha and argyrol injections, the symptoms yielded almost at once to injections of creosote of a similar strength. Although the breath smelt strongly of creosote for some time, the evidences of absorption were inconsiderable and the urine remained unaffected.

Other varieties of protozoan dysentery are treated locally in the same way as amœbic infections. For balantidian dysentery, rectal douches are generally sufficient, and the administration of drugs is unnecessary.

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<sup>2</sup> Bulletin, *Société de Pathologie Exotique*, ii., 1909.



## CHAPTER XXIII.

## SURGICAL AND OTHER METHODS OF TREATMENT.

IN the treatment of chronic amœbic dysentery surgical intervention is seldom desirable; but it may be necessary to have recourse to an operation in the following circumstances: (1) When a crisis, such as perforation, occurs; (2) to provide a more effective method of dealing with the lesions in the great intestine; (3) to relieve a patient from the permanent discomfort which is consequent on incurable disease, fibrosis, or dilatation of the colon. Trans-peritoneal operations are, however, justifiable only in extreme cases; and, except in the first instance, only after other means have failed to ameliorate an obstinate and possibly dangerous condition.

Three principal methods of remedial surgical treatment have been advocated. They are: (1) The formation of a temporary artificial anus in the cæcum, through which the dejecta may be passed for several weeks. It is presumed that, complete rest being thus assured to the colon, the ulcerated and disorganized mucosa will heal rapidly, and that the opening may then be successfully closed.

(2) Lavage of the intestine through the appendix vermiformis. An incision is made into the groin over the appendix, which is brought to the surface and anchored by silk sutures to the edge of the wound. The end having been cut off, the lumen is kept open, and a rubber catheter is passed through it into the intestine. In this way the colon may be freely and repeatedly douched by

medicated solutions, and the opening can be afterwards closed by resection of the appendix.

(3) Excision of the whole of the large intestine and anastomosis of the cut end of the ileum with the rectum.

The first operation—that of forming a comparatively large opening into the cæcum—although it provides an excellent opportunity for intestinal irrigation, and although numerous successful cases have been published,<sup>1</sup> is attended by so many disadvantages that it has now been practically abandoned. The irritation is greater and the general condition of the patient is even more pitiable than when an artificial opening is made into the sigmoid from the left groin; and extreme difficulty is almost invariably experienced in closing the opening.

In cases of chronic and apparently incurable dysentery STEINER<sup>2</sup> has recently employed the following method with marked success. After a large opening into the cæcum has been established, the colon is washed out daily *from below* with a weak solution of argyrol, the injection being continued until it flows clear from the cæcal incision. When the colon is healed the artificial anus is temporarily closed by tampons, and the dejecta are allowed to pass through the natural channel, the closure being afterwards made permanent if there is no return of symptoms.

The second method, in which the appendix is used as an opening for irrigation only—no attempt being made to divert the intestinal contents—is frequently adopted for the relief of malignant and other conditions of the colon, and has also been successfully employed in the treatment of amœbic dysentery. Unless there are

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<sup>1</sup> See among others, Dr. Simpson and Mr. Keith, *Medical Press and Circular*, July 29, 1896.

<sup>2</sup> *Berliner klinisch Wochenschrift*, February 8, 1908.

extensive adhesions, the operation presents no difficulty, and the appendix may generally be drawn out through a small wound. It is better to defer opening the appendix until union with the abdominal parietes is complete, generally about four days afterwards, but irrigation two or three times daily may then be undertaken almost at once. A cleansing douche of warm water should first be injected, and after it has been passed, two to three pints of argyrol, copper sulphate, or permanganate solution should be allowed to flow slowly into the cæcum. Both injections generally reach the rectum within ten minutes, but in order not to unduly hasten their transit the patient should be kept perfectly still. The rubber tube must be retained *in situ* so long as the appendix is open. KEETLEY, ARTHUR, and others, who have employed appendicostomy in numerous cases of chronic dysentery, speak<sup>3</sup> highly of the applicability and utility of this operation as a general method of treatment; but MILTON HOLT, who is equally convinced of the efficacy of the procedure, considers<sup>4</sup> that it should be undertaken only when entamœbæ persist in the dejecta after a year's trial of rectal irrigation. With this view most tropical physicians will agree; but it may be admitted that high ulceration in the ascending colon, which cannot be reached by injections from below, warrants earlier intervention than lesions which are situated in the sigmoid flexure.

The somewhat formidable operation of excision of the whole colon has been followed by brilliant results in the hands of Mr. ARBUTHNOT LANE and a few other surgeons, but there has been insufficient time for the accumulation of evidence as to the permanency of the relief which it affords. Those who are familiar

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<sup>3</sup> *Medical Record*, March 25, 1905.

<sup>4</sup> *New York Medical Journal*, November 16, 1907.

with the extremity of suffering to which a toxæmic patient may be reduced, and with the structural disorganization of the colon caused by advanced and neglected amœbic dysentery, will, however, have no difficulty in agreeing that this heroic measure may be the only alternative which offers any prospect of saving life, and that in such conditions it is eminently justifiable. The recorded mortality of the operation is abnormally high, for it is seldom undertaken before the patient is *in extremis*, and there can be no question that if excision of the colon is carried out earlier there will be a marked reduction in the percentage of fatalities.

It occasionally happens that amœbic infection persists in limited areas after the rest of the colon has healed ; and single ulcers which obstinately resist all treatment are by no means infrequent sequelæ of tropical dysentery. Callous ulceration of this type is generally attended by periodic attacks of acute pain ; in some instances, these are so severe that it may become necessary to explore the condition of the colon by laparotomy, and, if the diagnosis is confirmed, to excise the ulcer. Operative interference is, of course, unjustifiable unless the sections can be made through healthy intestine.

In view of their powerful amœbicide action *in vitro*, an attempt to destroy entamœbæ in the tissues by means of x-rays would appear to be a rational and feasible procedure. Numerous external affections dependent on the growth of trichophytons and other pathogenic organisms are now regularly treated in this way, and it is believed that deeper structures may be similarly influenced by radio-therapy. It is for instance claimed<sup>5</sup> that the progress of leukaemia, both splenic and myelogenous, may be arrested by the

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<sup>5</sup> Ledingham and McKerron, *Lancet*, January 14, 1905. Kienbock, *Lancet*, June 20, 1907.

direct application of x-rays to the spleen and bones, and that many other diseases,<sup>6</sup> including leprosy, may be similarly relieved.

There are as yet insufficient data to establish the therapeutic value of x-rays in amœbic dysentery, but at least one patient appears to have been cured in this way. It must not be forgotten that degeneration in healthy tissues is frequently induced by exposure to the rays, and De Courcelles states<sup>7</sup> that not only the testes and ovaries, but the whole of the intestinal lymph glands, may become atrophied as a result of this treatment.

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<sup>6</sup> See Heinecke, *Münchener med. Wochens.*, May 3, 1904; Senn, and others.

<sup>7</sup> Foveau de Courcelles, *La Semaine Méd.*, 1903, p. 364; 1905, p. 116.

## CHAPTER XXIV.

THE TREATMENT OF AMŒBIC ABSCESS OF THE LIVER.  
PROPHYLAXIS.

WITH improved methods of treatment, the case incidence and the mortality of hepatic suppuration have, in recent years, shown marked diminution, and still further progress in the prevention and cure of the gravest of all the sequelæ of intestinal amœbiasis may be anticipated in the future. It is now fully established that early identification of amœbic infection of the colon is the most important consideration in the prophylaxis of liver abscess; and that, when suppuration has taken place, timely surgical intervention is the surest means of effectively reducing the appalling fatality of the complication.

The amelioration in the incidence of metastatic abscess has, however, been materially assisted in other ways. Many factors contribute to the predisposition of liver tissue to suppuration; personal habits, tendency to dietetic and alcoholic excess, exposure to unwonted climatic conditions, psychic and mental causes, all exercise a powerful influence; and it is no doubt due in a great measure to changes in the methods of life which formerly prevailed in the tropics that there has been such a marked decrease in the frequency of the complication. Hepatic suppuration is, however, still far too common; and it is by no means the case, as is frequently asserted, that it occurs only when amœbic dysentery has been neglected or improperly treated.



A notable advance in the prevention of liver abscess has been recently made in Calcutta, where ROGERS has shown that remarkable reduction in the case incidence may be attained by the systematic employment of ipecacuanha as a prophylactic in the earliest stage of hepatic invasion.<sup>1</sup> Although the dysenteric symptoms were sometimes so mild as to be almost imperceptible, ROGERS found that, in 90 per cent. of his cases, there was a definite connection between the two conditions; and that the occurrence of polynuclear leucocytosis almost invariably foreshadowed the formation of an amœbic abscess. Therefore, whenever hepatitis, however slight, was attended by a marked excess of leucocytes, he concluded that he had to deal with a pre-suppurative stage of infection of the liver by intestinal amœbæ, and he prescribed ipecacuanha in large doses with the following results:—

In three cases of inflammation of the liver with leucocytosis, in all of which there was a history of dysentery, the fever and other evidences of hepatitis disappeared after from two to four days' treatment by ipecacuanha, although these symptoms had previously persisted for two, five, and six weeks, respectively. In three similar instances where the patients were not treated by ipecacuanha, fever subsided only after several weeks; whilst, in a further series of five cases in which large doses of the drug were administered, the temperature, which had been continuously high for more than a month, fell to normal in from one to six days. Further, three cases of fever, with polynuclear leucocytosis and slight enlargement of the liver, which exhibited no other evidence of amœbic infection, were cured by ipecacuanha in from two to fifteen days, after five, eight, and nine weeks' illness.

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<sup>1</sup> L. ROGERS: Paper read at the Annual Meeting of the Philippine Islands Medical Association, February 29, 1908.

Later results have confirmed the utility of this method of treatment, which—although previously recommended by CHEVERS, MACLEAN, and others—it has remained for ROGERS to bring into general use. In the Calcutta General Hospital for Europeans, no case of liver abscess occurred as a sequela of dysentery during two years after the introduction of the ipecacuanha treatment; and an equal measure of success has been attained in many other centres of amœbic infection.

So far, no clinical evidence has been adduced to show that similar methods of preventive treatment may be equally efficacious; but there can be no question that the success of the remedy depends on the destruction of the specific entamœbæ; and when ipecacuanha cannot be tolerated, benzosol and other germicides may be confidently expected to produce similar results. Palliative measures, such as the application of fomentations and counter-irritation over the liver, almost invariably fail to effect the slightest permanent improvement or to arrest the progress of suppuration; and the obvious indication afforded by these experiences is that in all cases of amœbic infection, especially when there is evidence of hepatic complication, or when obscure intestinal symptoms are combined with leucocytosis, specific antidysenteric remedies (both internal and local), should be prescribed early and continuously.

#### OPERATIVE TREATMENT.

On the formation of an abscess, steps must be taken to evacuate the pus; and thereafter to maintain free drainage of the cavity until it is healed. The determination of the actual condition is sometimes very difficult, and suppuration must be diagnosed rather by the general symptoms than by the physical signs. In no case should an operation be delayed until fluctuation can be elicited; for when that sign is obtained it is often too late to save the patient.

No reliance can be placed on aspiration as a method of treatment. In rare instances it may be sufficient to effect a cure, and combined with subsequent injection of quinine solution it is sometimes useful in dealing with small abscesses; but in the vast majority of cases free incision is necessary. Moreover, employed merely as a means of diagnosis, aspiration is by no means free from objection. Apart from the fact that irremediable damage may be done by injury to blood-vessels, hepatic pus is often so viscid that it will not flow through a needle, although it may afterwards extravasate along the track of the instrument into the peritoneal cavity.

Two operations are in common use—the first, or *abdominal*, being employed when the abscess is situated in the lower segments of the liver; the second, or *transsthoracic*, when the cavity lies in the external or superior portions of the gland, or extends upwards towards the thorax. Besides the appliances usually required for laparotomy, the following instruments should be provided: An exploring syringe or aspirator, a large trocar and cannula, a Paquelin's cautery, a periosteal elevator, a rib saw, a bone forceps, several large fully-curved threaded needles, and stout rubber drainage tubes. All surgical procedures are, of course, carried out with strict antiseptic precautions.

*The Abdominal Operation.*—After the usual preparation the patient is placed on the back, or when lateral incision is necessary, on the left side; and in order to raise the liver close up to the external wound a hard pillow or sandbag is inserted under the hollow of the spine. An incision through skin and subcutaneous tissue, 3 to 4 inches in length, is carried directly downwards from the lower border of the costal margin across the most prominent part of the swelling, and is gradually deepened until the peritoneum is reached. The existence of adhesions, less frequent in this position than where there is resistant rib-pressure, may now be

determined. If the tissues are thickly matted together and the peritoneal cavity is thus shut off from the wound, the abscess may be evacuated as soon as its nearest point is located. On the other hand, when there are no adhesions, the peritoneum must be carefully opened, the liver being freely exposed by drawing asunder the edges of the incision. Flat sponges are gently packed between the liver and the abdominal walls so as to form a complete circle round the opening and dam off the cavity of the peritoneum from contamination by the contents of the abscess. The liver must not be incised until this has been done.

Incision of inflamed liver tissue is always attended by the risk of severe hæmorrhage, and it is important that the abscess should be reached at the point where it is most superficial. Before section, therefore, an endeavour should be made to determine as closely as possible the actual position of the cavity, an exploring syringe or trocar being, if necessary, used for the purpose. When found, the abscess is opened by the trocar, the aperture being afterwards carefully enlarged by the blades of a dressing forceps; or if deeply situated in liver tissue, by a Paquelin cautery at a dull red heat. During evacuation the abdominal walls must be kept gently pressed down on the liver, so as to maintain complete occlusion of the peritoneum and assist the discharge of pus.

Free drainage can seldom be secured in the case of a large abscess, unless the opening in the liver admits two fingers; and when the incision has been increased to that size, a fairly rigid rubber drainage tube of large calibre should be passed in, the cavity being freely irrigated by hot water, or by a solution (1 in 2,000 water) of bisulphate of quinine dissolved in weak sulphuric acid. So far as is practicable, the cavity ought also to be explored by the finger, and its extent and the existence of other abscesses determined.

The most important part of the operation—the provision of

drainage without peritoneal contamination—still remains to be accomplished. The rubber tube being left *in situ*, the whole length of the wound in the liver is packed round it with a single ribbon of iodoform gauze, so that although free exit is provided for the pus *through* the lumen there can be no leakage along the outer circumference of the pipe. The flat sponges are now carefully removed, after irrigation of their surfaces, and the wound is filled up with gauze. The drainage tube may with advantage be cut short, and its mouth anchored by two stitches to the edges of the skin. The wound is afterwards covered by a large pad of absorbent wool and protective tissue.

If, after packing the tube, there is still danger of leakage, the margins of the abdominal and liver incisions should be united by a ring of interrupted silk sutures placed not more than a quarter of an inch apart. Satisfactory union may generally be effected by entering curved threaded needles deep in the hepatic tissue, and directing them upwards and outwards so as to reach the surface of the liver half an inch from the opening; they are then carried directly onwards through the abdominal wall until they emerge close to the edge of the external incision, when the sutures are released from the needles, and the ends are tied.

If the abscess is small, packing the cavity by soft gauze may be substituted for a rubber drainage tube. A gauze dressing has, in itself, many advantages; it is unlikely to injure the liver during sharp movements such as are caused by coughing or vomiting, and its own capillary attraction assists in maintaining drainage. In many cases, as, for instance, when there is a tendency to hæmorrhage from the wound or from the abscess walls, gauze packing may be indispensable, for by no other means can bleeding or oozing be so promptly and completely arrested. The use of gauze, however, entails frequent irrigation and changes of deep dressing,

and when the cavity is large these procedures are so tedious and exhausting that better results can generally be obtained by tube drainage.

*Transthoracic Operations.*—Abscesses situated in the upper portion of the liver can seldom be satisfactorily treated unless part of a rib is resected, as, with the evacuation of the cavity, the intercostal spaces rapidly decrease in size, and drainage tubes are occluded by pressure. The natural width of these spaces, however, varies considerably. In some cases a rigid metal tube of moderate size causes little or no inconvenience, and I have successfully treated many high abscesses by means of a simple pattern of silver irrigating cannula, kept permanently *in situ* between the ribs. The cannula slides stiffly through a shield by which it is retained in position, being thus shortened at will; and after irrigation of the cavity it is attached to a syphon drainage tube which discharges into a jar of carbolic solution placed below the patient's bed.

When there is extensive disorganization of hepatic tissue, however, trocar-drainage affords little prospect of providing sufficient exit for the discharges, and it is necessary to have recourse to more radical measures. In such circumstances, excision of part of one or more ribs is generally advisable; and, when the abscess appears to be a large one, that operation should be undertaken without waiting for the result of an attempt at relief by less effective methods. The incision may be made above the insertion of the diaphragm, in which case the opening is actually transthoracic; but it is usual to include in the same term operations which involve resection of a rib below that level. Whether the pleural or peritoneal cavity is traversed, the procedure is practically the same.

*The Operation.*—The hepatic area is fully exposed by placing a sandbag under the hollow of the spine, and turning the patient across it in a semi-prone position to the left. After determining the



probable position of the abscess by inspection and palpation, the rib which appears to be most widely separated from its fellows by bulging intercostal spaces is selected ; and an incision,  $3\frac{1}{2}$  to 4 in. in length, is made parallel to the edges of the bone, and along its median line. The incision should be clean and deep ; that is to say, it should divide skin, muscular tissue, fasciæ, and periosteum. Bleeding points having been arrested by pressure forceps, the edges of the wound are held apart, and the periosteum is freely separated from both aspects of about 3 in. of bone by means of a periosteal elevator.

The rib is then cut across at each end of the denuded space by a bone forceps, or preferably by a small saw. After removal of the divided segment, the costal pleura is opened by a probe-pointed director and the blades of a dressing-forceps, the visceral pleura being thus brought freely into view. At this stage, air pressure from without generally causes partial collapse of the exposed lung, and the pleura overlying the diaphragm may be clearly seen. In most cases, also, the pressure of pus in the liver causes it to bulge up into the wound, and there is then no difficulty in determining the position of the abscess ; but, in some instances, the use of an aspirator may be necessary.

Before incising the diaphragm, however, the thoracic cavity (if uninfected by pus) must be shut off from the wound by uniting the margins of the costal and diaphragmatic pleura. Closely-set interrupted sutures of fine silk are passed through an incision in the deeper serous layer corresponding to the opening in the costal pleura, and the stitches, after being carried through that structure, are tied in a complete circle round the track of the wound. If the pleural cavity is already suppurating, no attempt should be made to close it ; but, on the contrary, free exit should be given to the purulent fluid by gentle irrigation, the insertion of a soft drainage

tube, and the application of large pads of absorbent gauze. The diaphragm should not be attached to the thoracic wall, as the stitches are apt to be torn asunder by sudden movements such as are induced by coughing or retching.

As a rule there is no necessity to cut or tie the intercostal arteries. These vessels lie well away from the periosteal sheath; and if the elevator is kept inside that structure they can scarcely be injured when a portion of only one rib is removed. It sometimes happens, however, that in order to secure a sufficient opening, two ribs must be resected, and it is then necessary to cut away the periosteum as well as the bone. In such a case, the larger branch of the artery, which lies between the outer and inner intercostal muscles, behind the lower sharp border of the rib, should be tied at both ends of the proposed incision by a ligature passed round it by means of an aneurism needle. The smaller branch—on the upper border of the rib—may generally be secured by pressure or by a twist from an artery forceps.

The diaphragm being thus exposed, and the pleural cavity shut off from the wound, an incision is made directly into the hepatic tissue, and is gradually deepened until the cavity is reached. The abscess may then be evacuated and drained in the usual way.

Although in most cases the structures heal rapidly, convalescence after an operation for abscess of the liver is prolonged and unsatisfactory. The exhaustion and secondary anæmia incident to protracted suppuration of the hepatic tissue is of an unusually severe type, and recovery is generally tedious and marked by frequent interruptions. European patients on whom the operation has to be carried out in the tropics should be sent home as soon as they are able to travel; and in such circumstances it is more than questionable whether they should ever again attempt to live in a hot climate.

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